



# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier

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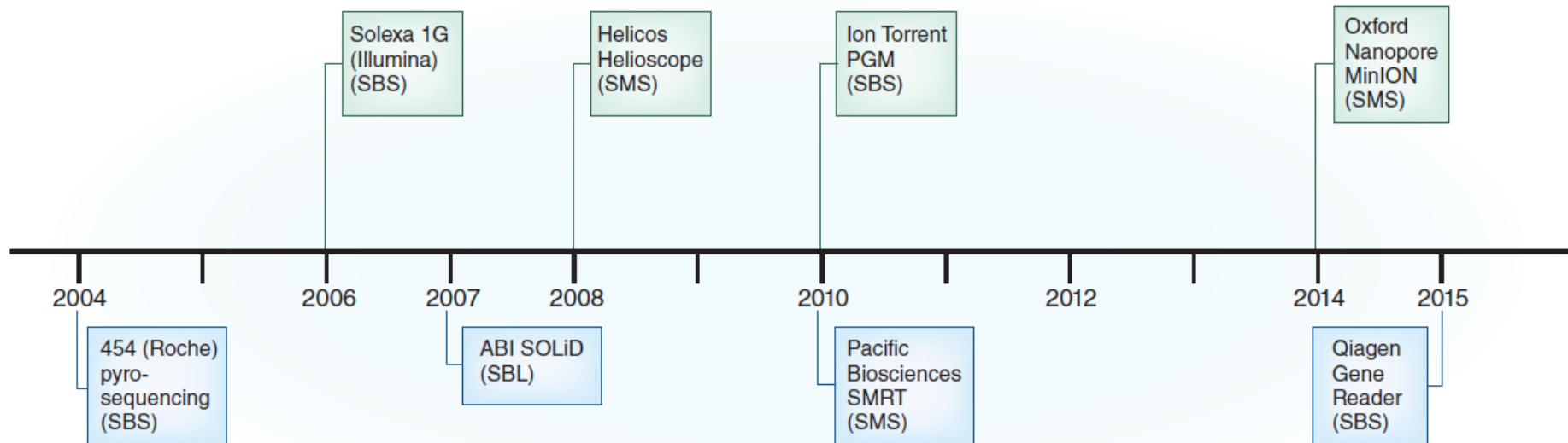
Universität Bern

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25. September 2018, Berner Kolloquien für Labormedizin

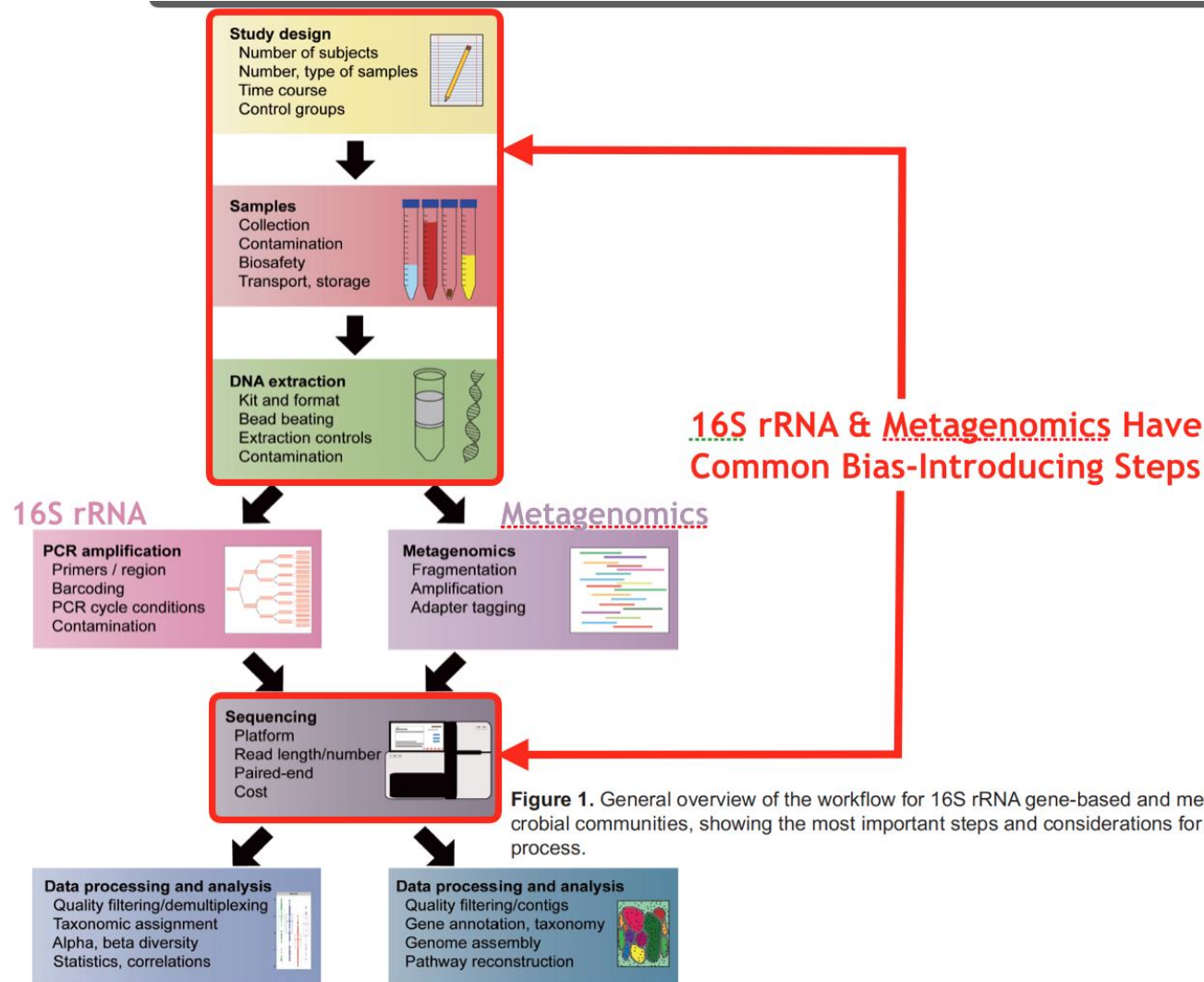
- Metagenomics: mit molekularbiologischen Methoden die Gesamtheit des Genoms eines Biotops erfassen. Zu diesem Genom gehören alle Mikroorganismen, aber auch die Wirts-DNA → Mikrobiom
  - **Datenschutz!**
- Next generation sequencing (Sanger Sequenzierung 1., ab 2004 NGS)
- Amplikonsequenzierung: Sequenzierung von Fragmenten, die mittels PCR amplifiziert wurden = Amplikone; z.B. 16S rRNA Gen, 18S rRNA Gen, Internal Transcribed Spacer (ITS) → Mikrobiota
- Metagenomics → Shotgun-Sequenzierung:
  - „Schrotschuss-Sequenzierung“ ist in der Molekularbiologie eine Methode zur Sequenzierung langer DNA-Stränge

# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier



**Figure 1** | NGS instruments introduced over the past decade. This timeline describes the year of introduction of each of the NGS platforms that successfully achieved commercial introduction during the past decade. SBS, sequencing by synthesis; SMS, single-molecule sequencing; SBL, sequencing by ligation.

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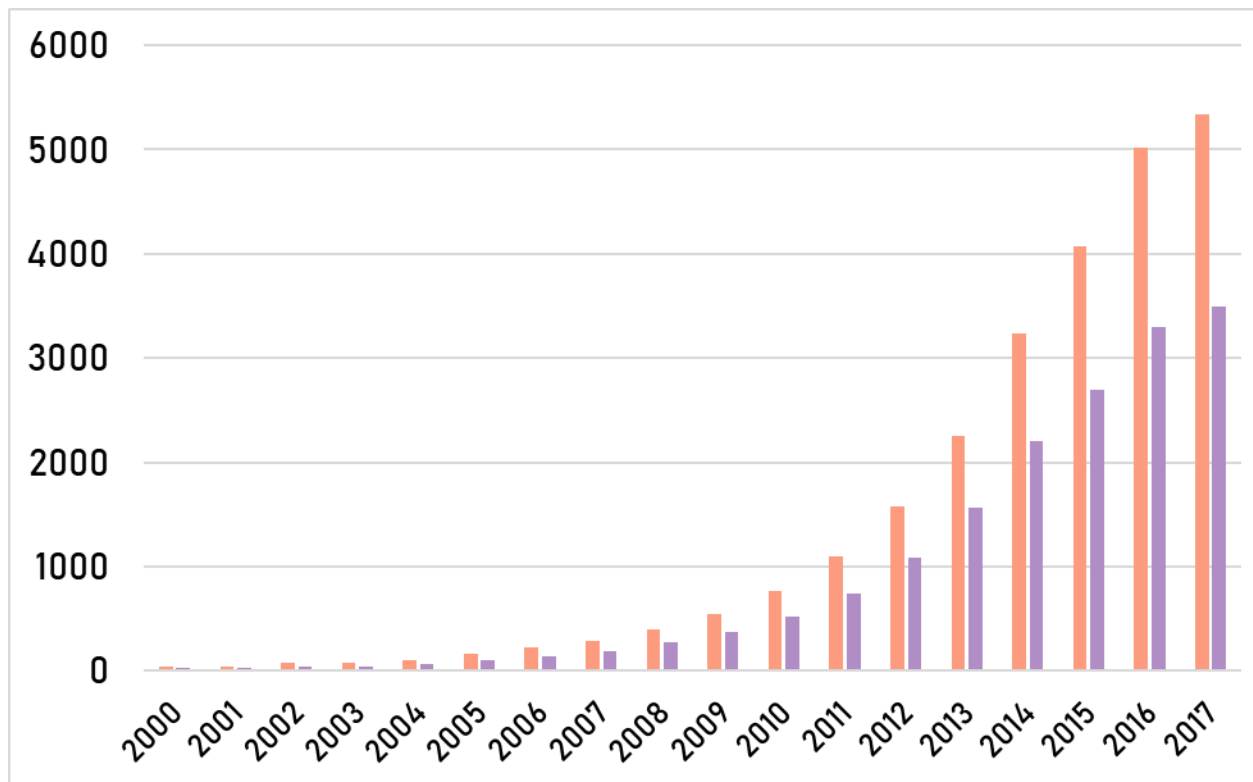


**Figure 1.** General overview of the workflow for 16S rRNA gene-based and metagenomic analysis of microbial communities, showing the most important steps and considerations for each stage of the process.

# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier

- Publikationen zum **Humanmikrobiom** und **Tiermikrobiom**

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# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier

- Schnittstelle Mensch – Tier

60% of existing human infectious diseases are zoonotic



At least 75% of emerging infectious diseases of humans (including Ebola, HIV, and influenza) have an animal origin



5 new human diseases appear every year. Three are of animal origin



80% of agents with potential bioterrorist use are zoonotic pathogens



<http://www.oie.int/en/for-the-media/onehealth/>

# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier

Antibiotika-  
resistenz



Nutztiere



Zoonosen



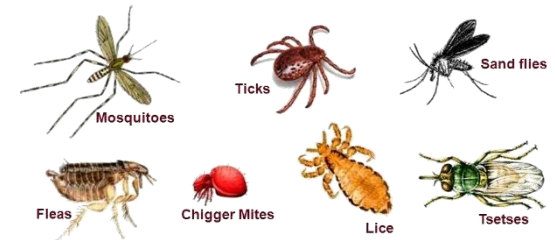
Produktion

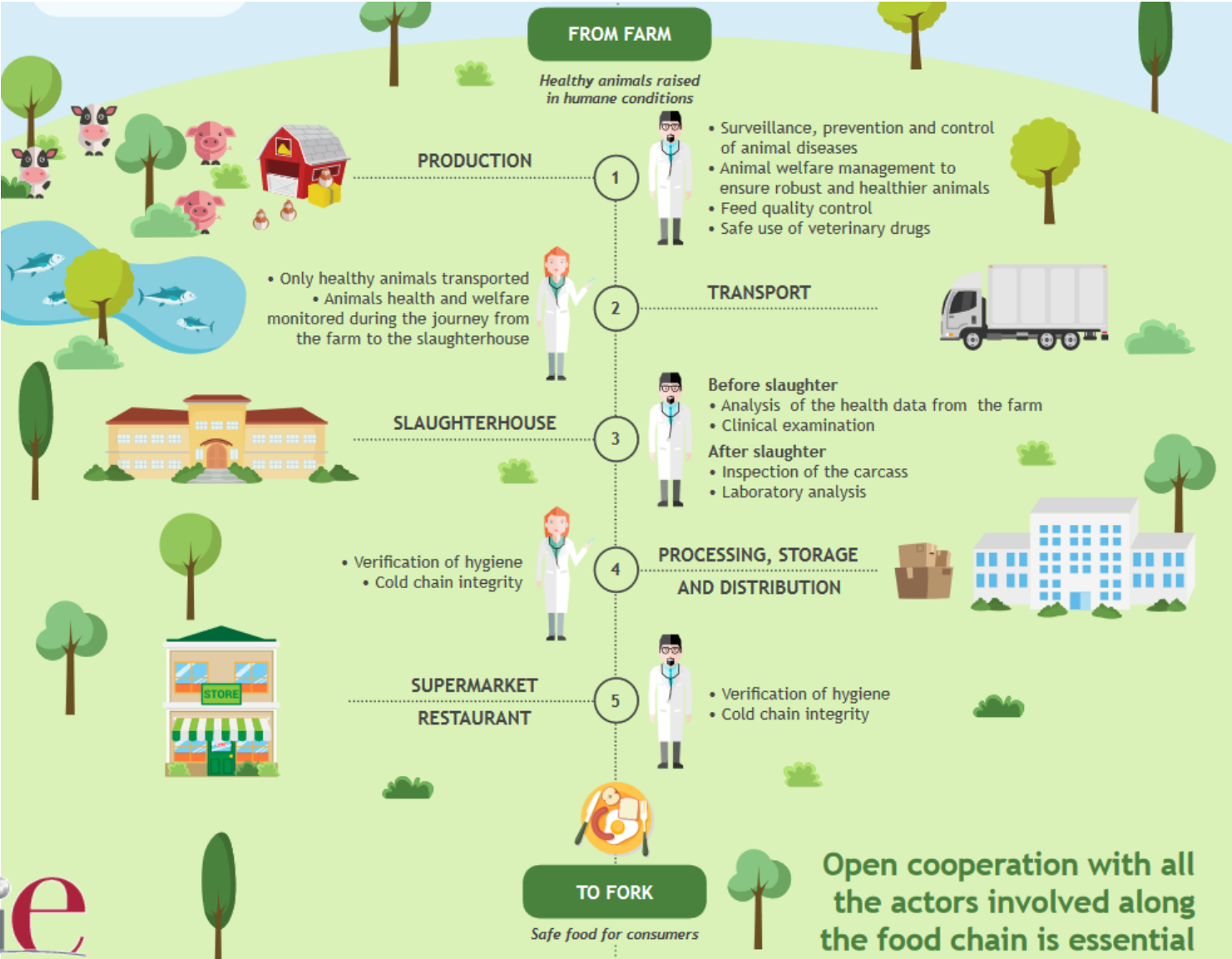


Tiermodell



Vektoren







## Zoonosen

• Zoonosen; Tierseuchenverordnung SR: 916.401  
<https://www.blv.admin.ch/blv/de/home/tiere/tierseuchen/uebersicht-seuchen/zoonosen.html>

- |                                         |                                           |                              |
|-----------------------------------------|-------------------------------------------|------------------------------|
| • Aktinomykose                          | • Listeriose                              | • Sarkosporidiose            |
| • Brucellose                            | • Louping III                             | • Staphylococcus-Infektionen |
| • BSE und Creutzfeldt-Jakob Disease     | • Milzbrand                               | • Tollwut                    |
| • Campylobacteriose                     | • Newcastle-Krankheit                     | • Toxoplasmose               |
| • Chlamydienabort der Schafe und Ziegen | • Nipahvirus-Enzephalitis                 | • Trichinellose              |
| • Chlamydiose der Vögel                 | • Paratuberkulose / Morbus Crohn          | • Tuberkulose                |
| • Clostridien-Gastroenteritis           | • Pferdeenzephalomyelitiden               | • Tularämie                  |
| • Coxiellose                            | • Pseudotuberkulose der Schafe und Ziegen | • Vesikuläre Stomatitis      |
| • Cryptosporidiose                      | • Rifttalfieber                           | • Vogelgrippe                |
| • Echinococcose                         | • Rotlauf                                 | • West-Nil Fieber            |
| • EHEC                                  | • Rotz / Malleus                          | • Yersiniose                 |
| • Frühsommer-Meningoencephalitis FSME   | • Salmonellose und Salmonella-Infektion   | • Zystizerkose               |
| • Hendra Virus                          |                                           |                              |
| • Leptospirose                          |                                           |                              |

- Zoonosen; Tierseuchenverordnung SR: 916.401

<https://www.blv.admin.ch/blv/de/home/tiere/tierseuchen/uebersicht-seuchen/zoonosen.html>

- |                                                |                                                |                                     |
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| • Aktinomykose                                 | • Listeriose                                   | • Sarkosporidiose                   |
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| • Hendra Virus                                 |                                                |                                     |
| • <u>Leptospirose</u>                          |                                                |                                     |

Vidal et al. *Vet Res* (2017) 48:64  
DOI 10.1186/s13567-017-0470-1



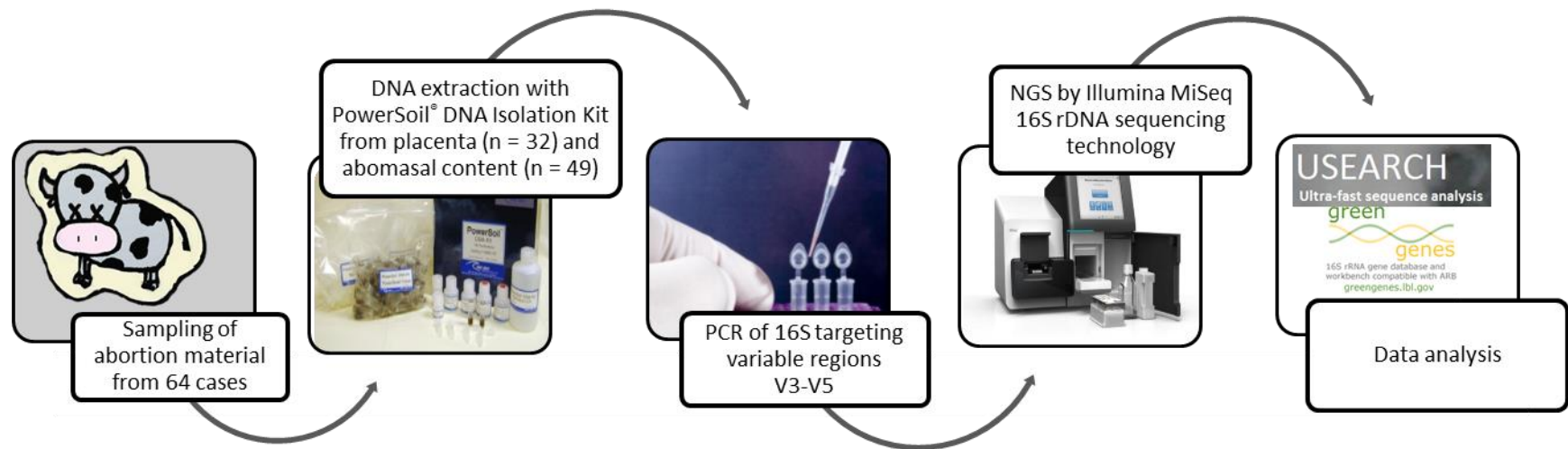
RESEARCH ARTICLE

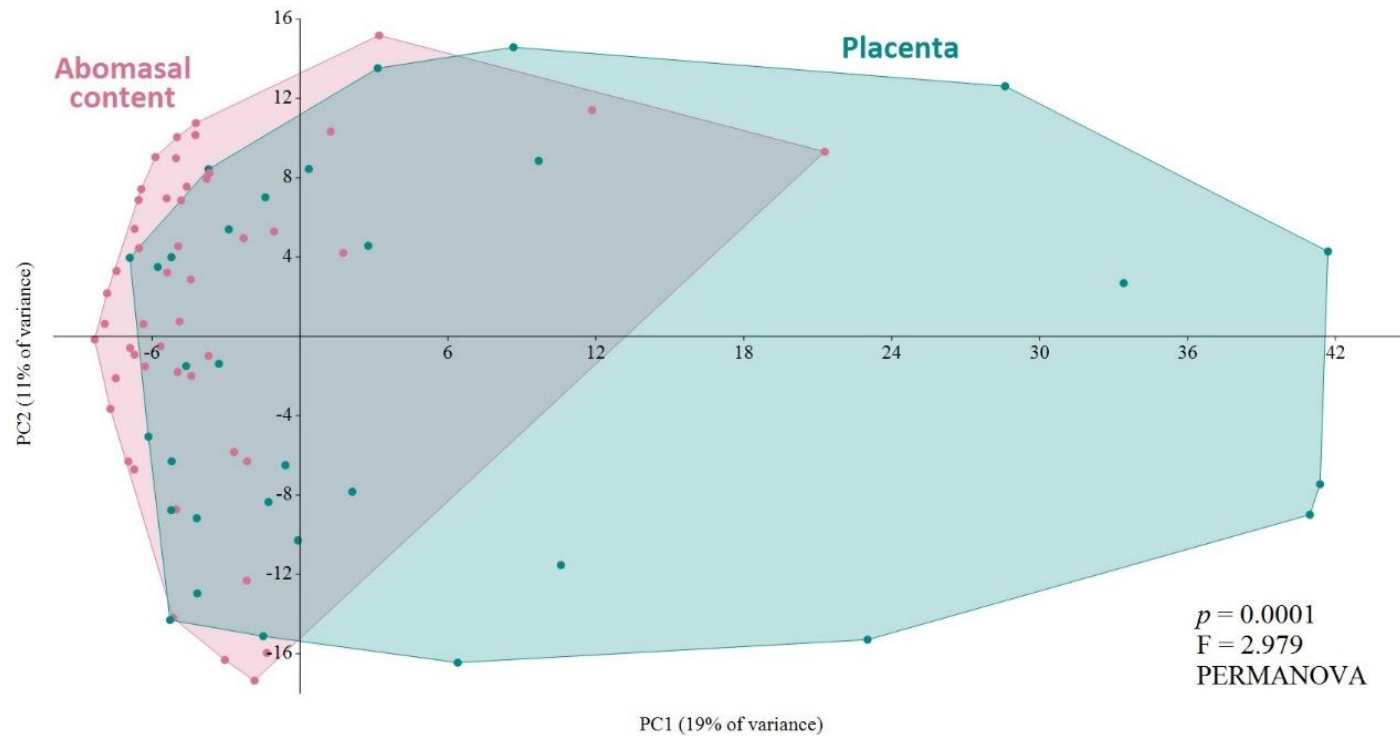
Open Access



# Amplicon sequencing of bacterial microbiota in abortion material from cattle

Sara Vidal<sup>1,2</sup>, Kristel Kegler<sup>3</sup>, Horst Posthaus<sup>3</sup>, Vincent Perreten<sup>1</sup> and Sabrina Rodriguez-Campos<sup>1\*</sup>





**Figure 1** Two-dimensional ordination of the microbial profiles of the abomasal content and placenta by principal component analysis (PCA). Significant differences;  $p < 0.01$ , PERMANOVA.

**Table 3 Comparison of histopathological analysis and most abundant genera found by next generation sequencing (NGS) in available placenta samples**

| Sample ID   | Placentitis | Necrosis | Type of infiltrate | Vasculitis | Presence of ICB <sup>a</sup> | Presence of ECB <sup>b</sup> | Most abundant genera found by NGS (≤ 75% of the reads)                                                                                                                                                                                                                                                                                                   | Comments                                                                                                    |
|-------------|-------------|----------|--------------------|------------|------------------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| 12Ue1096_PI | Mild        | Mild     | Mixed              | Yes        | Yes                          | Yes                          | <i>Pseudomonas</i> (86.72%), others (13.28%)                                                                                                                                                                                                                                                                                                             |                                                                                                             |
| 12Ue1503_PI | No          | Moderate | No                 | No         | No                           | Yes                          | <i>Pseudomonas</i> (91.26%), others (8.74%)                                                                                                                                                                                                                                                                                                              | <i>Pseudomonas</i> (99.68%) in the abomasal content                                                         |
| 13Ue218_PI  | No          | No       | No                 | No         | No                           | Yes                          | <i>Clostridium</i> (29.94%), <i>Enterococcus</i> (9.71%), <i>Ruminococcaceae</i> <sup>a</sup> (9.67%), <i>Flavobacterium</i> (6.89%), <i>Bacteroidales</i> <sup>b</sup> (5.18%), <i>Enterobacteriaceae</i> (4.46%), <i>Pseudomonas</i> (3.32%), <i>Succinivibrio</i> (2.88%), <i>RF16</i> (2.43%), others (22.63%)                                       |                                                                                                             |
| 13Ue238_PI  | NA          | NA       | NA                 | NA         | NA                           | NA                           | <i>Psychrobacter</i> (30.22%), <i>Shewanella</i> (29.58%), <i>Flavobacteriales</i> <sup>b</sup> (12.76%), <i>Pseudomonadaceae</i> <sup>a</sup> (4.50%), others (22.94%)                                                                                                                                                                                  | Severe autolysis                                                                                            |
| 13Ue491_PI  | Mild        | Moderate | Mononuclear        | No         | No                           | No                           | <i>Bacteroides</i> (39.09%), <i>Pseudomonas</i> (26%), <i>Shewanella</i> (21.69%), others (13.22%)                                                                                                                                                                                                                                                       |                                                                                                             |
| 13Ue851_PI  | Moderate    | Moderate | Neutrophilic       | Yes        | No                           | No                           | <i>Enterobacteriaceae</i> <sup>a</sup> (46.46%), <i>Enterobacteriales</i> <sup>b</sup> (24.33%), <i>Serratia</i> (16.14%), others (13.07%)                                                                                                                                                                                                               |                                                                                                             |
| 13Ue1008_PI | Moderate    | Moderate | Mixed              | Yes        | No                           | Yes                          | <i>Vibrio</i> (89.92%), others (10.08%)                                                                                                                                                                                                                                                                                                                  | <i>V. metschnikovii</i> isolated in culture                                                                 |
| 13Ue1137_PI | Moderate    | Moderate | Mixed              | Yes        | No                           | Yes                          | <i>Streptococcus</i> (99.33%), others (0.67%)                                                                                                                                                                                                                                                                                                            | <i>Streptococcus</i> (99.62%) in the abomasal content, <i>S. uberis</i> isolated in culture                 |
| 13Ue1143_PI | Mild        | Mild     | Neutrophilic       | No         | No                           | Yes                          | <i>Enterobacteriaceae</i> <sup>a</sup> (96.19%), others (3.81%)                                                                                                                                                                                                                                                                                          | <i>Enterobacteriaceae</i> <sup>a</sup> (99.17%) in the abomasal content. <i>E. coli</i> isolated in culture |
| 13Ue1218_PI | Mild        | Mild     | Mixed              | Yes        | No                           | Yes                          | <i>Clostridium</i> (28.33%), <i>Cetobacterium</i> (13.16%), <i>Enterobacteriaceae</i> <sup>a</sup> (13.02%), <i>Peptostreptococcaceae</i> <sup>a</sup> (12.42%), <i>Aeromonadaceae</i> <sup>a</sup> (9.8%), others (23.27%)                                                                                                                              | High level of contamination with plants and feces                                                           |
| 13Ue1275_PI | Mild        | Mild     | Mixed              | Yes        | No                           | No                           | <i>Streptococcus</i> (37.24%), <i>Enterobacteriaceae</i> <sup>a</sup> (25.92%), <i>Lactococcus</i> (21.27%), others (15.57%)                                                                                                                                                                                                                             | <i>S. uberis</i> isolated in pure culture                                                                   |
| 13Ue1631_PI | NA          | NA       | NA                 | NA         | NA                           | NA                           | <i>Pseudomonadales</i> <sup>b</sup> (16.87%), <i>Pseudomonadaceae</i> <sup>a</sup> (16.24%), <i>Propionibacteriaceae</i> <sup>a</sup> (11.03%), <i>Acinetobacter</i> (9.13%), <i>Aeromonadaceae</i> <sup>a</sup> (6.81%), <i>Candidatus Portiera</i> (5.66%), <i>Ruminococcaceae</i> <sup>a</sup> (3.62%), <i>Psychrobacter</i> (3.33%), others (23.34%) | Severe autolysis                                                                                            |
| 13Ue1644_PI | No          | No       | No                 | No         | No                           | No                           | <i>Psychrobacter</i> (83.99%), others (16.01%)                                                                                                                                                                                                                                                                                                           |                                                                                                             |
| 13Ue1714_PI | NA          | NA       | NA                 | NA         | NA                           | NA                           | <i>Actinobacillus</i> (38.74%), <i>Clostridium</i> (15.78%), <i>Streptococcus</i> (14.54%), <i>Enterobacteriaceae</i> <sup>a</sup> (7.83%), others (23.11%)                                                                                                                                                                                              | Severe autolysis                                                                                            |
| 13Ue1756_PI | NA          | NA       | NA                 | NA         | NA                           | NA                           | <i>Psychrobacter</i> (33.24%), <i>Pseudomonadaceae</i> <sup>a</sup> (15.06%), <i>Aeromonadaceae</i> <sup>a</sup> (13.06%), <i>Acinetobacter</i> (12.23%), <i>Vibrio</i> (5.53%), others (20.88%)                                                                                                                                                         | Severe autolysis                                                                                            |
| 14A20_PI    | Mild        | Mild     | Mixed              | No         | No                           | Yes                          | <i>Aeromonadaceae</i> <sup>a</sup> (73%), <i>Pseudomonas</i> (26.26%), others (0.74%)                                                                                                                                                                                                                                                                    |                                                                                                             |
| 14A28_PI    | NA          | NA       | NA                 | NA         | NA                           | NA                           | <i>Shewanella</i> (24.04%), <i>Camomonas</i> (17.94%), <i>Psychrobacter</i> (9.97%), <i>Pseudomonadaceae</i> <sup>a</sup> (8.82%), <i>Pseudomonas</i> (4.49%), <i>Acinetobacter</i> (4.5%), <i>Wautersiella</i> (3.66%), <i>Staphylococcus</i> (3.64%), others (22.94%)                                                                                  | Severe autolysis                                                                                            |

Cases with positive results for parasitology, virology and/or with presence of intralesional fungal organisms were not included.

<sup>a</sup> Presence of intracytoplasmic bacteria (ICB).

<sup>b</sup> Presence of extracellular bacteria (ECB).

■ Läsionen vorhanden und > 70% der *reads* können einem Genus zugeordnet werden

### Nachteile NGS:

- sichere Zuordnung nur auf Genusebene, da Teilanalyse des 16S rRNA Gens
- Evtl. nicht alle Genera



Vidal et al. BMC Veterinary Research (2017) 13:373  
DOI 10.1186/s12917-017-1294-y

BMC Veterinary Research

### RESEARCH ARTICLE

Open Access



## Neglected zoonotic agents in cattle abortion: tackling the difficult to grow bacteria

Sara Vidal<sup>1,2</sup>, Kristel Kegel<sup>3</sup>, Gilbert Greub<sup>4</sup>, Sebastian Aebly<sup>4</sup>, Nicole Borel<sup>5</sup>, Mark P. Dagleish<sup>6</sup>, Horst Posthaus<sup>3</sup>, Vincent Perreten<sup>1</sup> and Sabrina Rodriguez-Campos<sup>1</sup>✉



Contents lists available at [ScienceDirect](#)

## International Journal of Surgery Case Reports

journal homepage: [www.casereports.com](http://www.casereports.com)



### Streptococcus pluranimalium: A novel human pathogen?

Lasanthi Aryasinghe<sup>a,\*</sup>, Saweera Sabbar<sup>a</sup>, Yasmin Kazim<sup>a</sup>, Liaqat Mahmood Awan<sup>b</sup>,  
Hammad Khan Nadir Khan<sup>a</sup>

<sup>a</sup> Department of Emergency Medicine, Rashid Hospital Trauma Center, Dubai, United Arab Emirates

<sup>b</sup> Department of Neurosurgery, Rashid Hospital Trauma Center, Dubai, United Arab Emirates



## Streptococcus pluranimalium: Emerging Animal Streptococcal Species as Causative Agent of Human Brain Abscess

Ganesh Maher<sup>1</sup>, Manish Beniwal<sup>2</sup>, Veenakumari Bahubali<sup>1</sup>, Shamick Biswas<sup>3</sup>, Nandeesh Bevinahalli<sup>4</sup>,  
Dwarakanath Srinivas<sup>2</sup>, Nagarathna Siddaiah<sup>1</sup>

## Multilocus Sequence Analysis of Streptococcus canis Confirms the Zoonotic Origin of Human Infections and Reveals Genetic Exchange with Streptococcus dysgalactiae subsp. equisimilis

M. D. Pinho,<sup>a</sup> S. C. Matos,<sup>a</sup> C. Pomba,<sup>b</sup> A. Lübke-Becker,<sup>c</sup> L. H. Wieler,<sup>c</sup> S. Prezioso,<sup>d</sup> J. Melo-Cristino,<sup>a</sup> M. Ramirez<sup>a</sup>

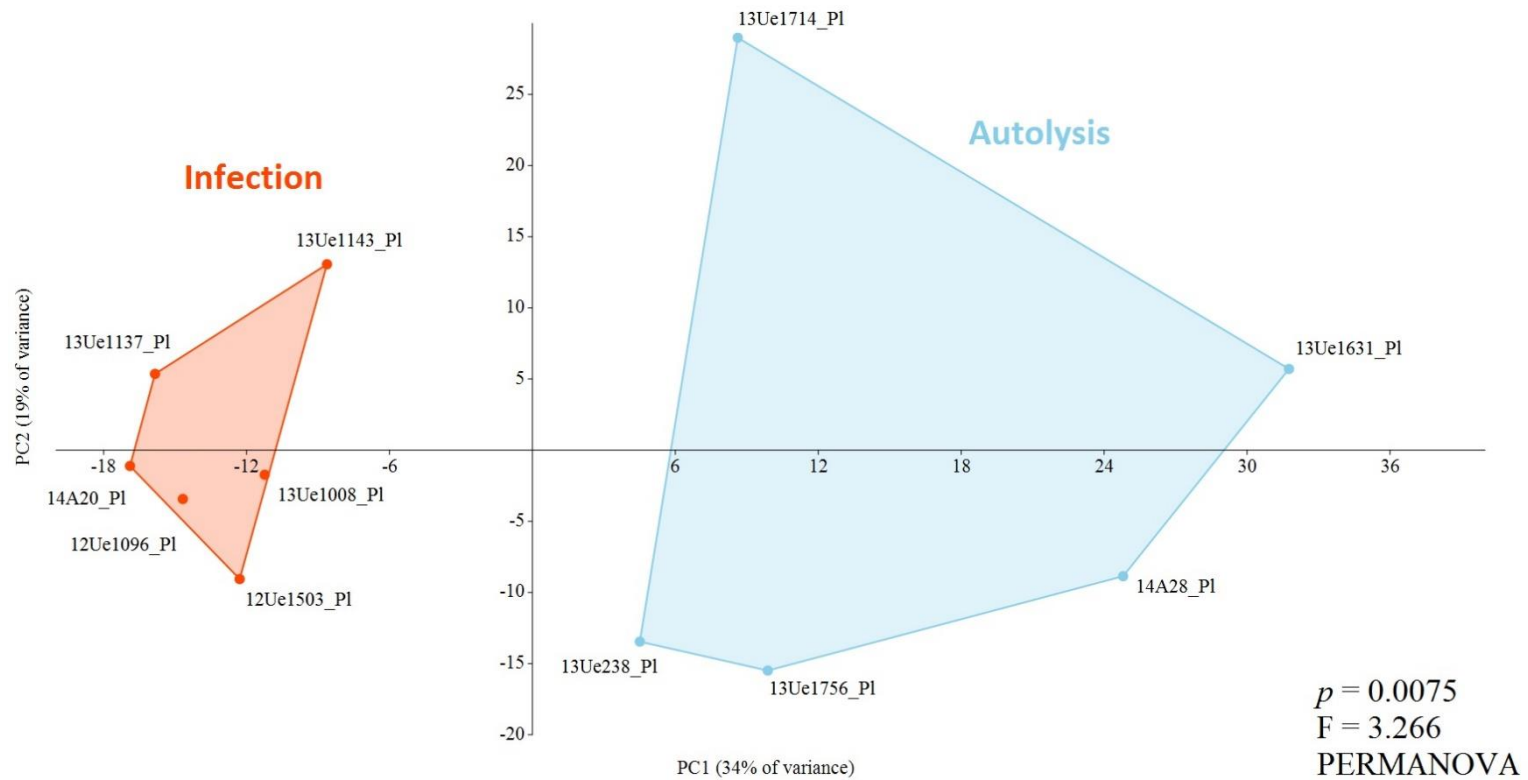
Instituto de Microbiologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal<sup>a</sup>; Centro Interdisciplinar em Sanidade Animal, Faculdade de Medicina Veterinária da Universidade Técnica de Lisboa, Lisbon, Portugal<sup>b</sup>; Institute of Microbiology and Epizootics, Veterinary Faculty, Freie Universität Berlin, Berlin, Germany<sup>c</sup>; Department of Veterinary Medical Sciences, University of Camerino, Matelica,

### RESEARCH ARTICLE

### Open Access

## Genome characterization and population genetic structure of the zoonotic pathogen, Streptococcus canis

Vincent P Richards<sup>1</sup>, Ruth N Zadoks<sup>2,4</sup>, Paulina D Pavinski Bitar<sup>1</sup>, Tristan Lefébure<sup>1,5</sup>, Ping Lang<sup>6</sup>, Brenda Werner<sup>2</sup>, Linda Tikofsky<sup>2,7</sup>, Paolo Moroni<sup>2,3</sup> and Michael J Stanhope<sup>1\*</sup>



**Figure 6 Two-dimensional ordination of the microbial profiles of the placentas presenting infection or autolysis by principal component analysis (PCA).** Significant differences;  $p < 0.01$ , PERMANOVA.

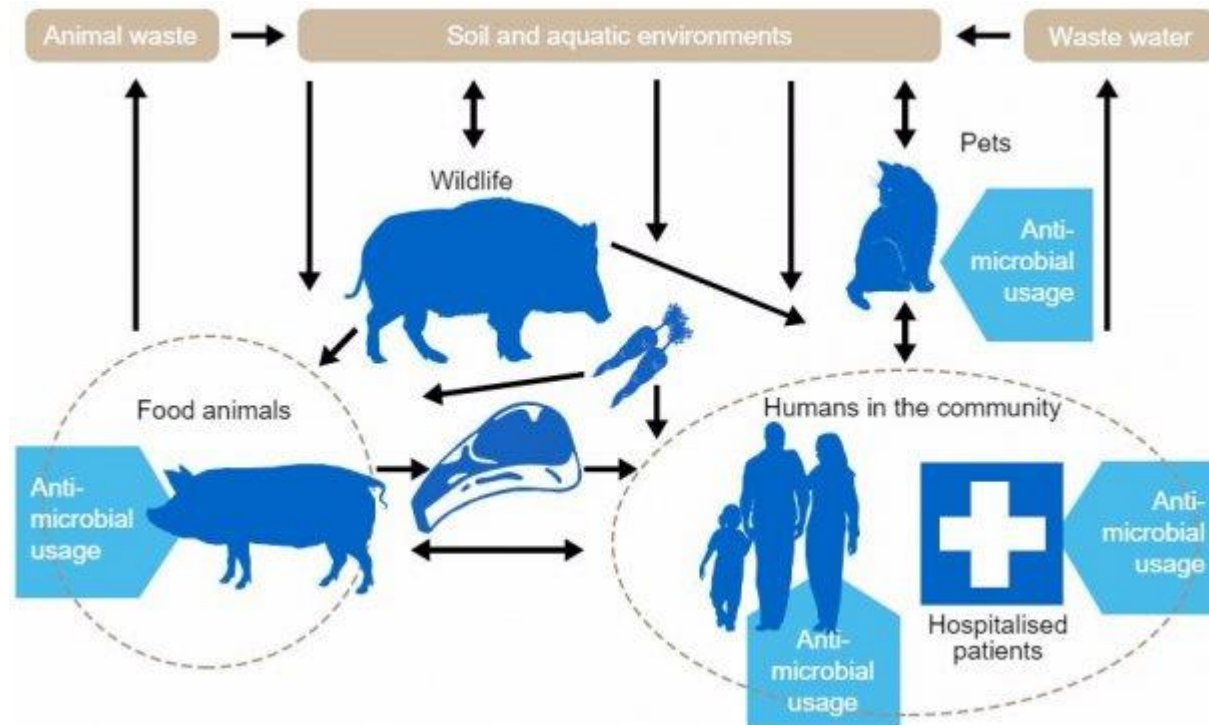


- Als Screeningmethode für vernachlässigte Erreger geeignet
- Für die Überwachung konkreter Zoonosen sind spezifische Methoden besser geeignet
- Zustand der Proben ist wichtig



- Zählt zu den grössten Gefahren für die Gesundheit des Menschen (WHO, 2014)
- Antibiotikaresistenzgene [antimicrobial resistance (AMR) genes] sind weitverbreitet in der Umwelt, auf allen Lebewesen und auf Lebensmitteln
- Austausch von genetischem Material → Erwerb von AMR
- Es ist wichtig, den Ursprung der AMR und die Übertragungswege auf den Menschen zu verstehen

# Antibiotikaresistenz



Flow diagram of antibiotic resistance determinants among the different reservoirs. Blue indicates points of antibiotic administration. <http://www.effort-against-amr.eu/>

- Zahlreiche Beispiele für die Übertragung von AMR in beide Richtungen  
Tier-Mensch, Mensch-Tier in der Literatur
- Meistens nur 1 konkreter Keim



Longitudinal study on the colonisation and transmission of methicillin-resistant *Staphylococcus aureus* in pig farms

Patrick Daniel Bangerter<sup>a</sup>, Xaver Sidler<sup>b</sup>, Vincent Perreten<sup>a</sup>, Gudrun Overesch<sup>a,\*</sup>

<sup>a</sup> Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern, Länggassstrasse 122, CH-3012 Bern, Switzerland

<sup>b</sup> Department of Farm Animals, Division of Swine Medicine, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 260, CH-8057 Zurich, Switzerland



## Highly Tigecycline-Resistant *Klebsiella pneumoniae* Sequence Type 11 (ST11) and ST147 Isolates from Companion Animals

Cristina M. Ovejero,<sup>a</sup> Jose Antonio Escudero,<sup>a</sup> Daniel Thomas-Lopez,<sup>a</sup> Andreas Hoefer,<sup>a</sup> Gabriel Moyano,<sup>a</sup> Natalia Montero,<sup>a</sup> Carmen Martin-Espada,<sup>a,b</sup> Bruno Gonzalez-Zorn<sup>a</sup>

Department of Animal Health and Centro de Vigilancia Sanitaria Veterinaria, Universidad Complutense de Madrid, Madrid, Spain<sup>a</sup>; Hospital Clínico Veterinario, Universidad Complutense de Madrid, Madrid, Spain<sup>b</sup>

- Zahlreiche Beispiele für die Übertragung von AMR in beide Richtungen

## Tier-Mensch, Mensch-Tier in der Literatur

### Prevalence of extended-spectrum $\beta$ -lactamase-producing *Enterobacteriaceae* and Methicillin-Resistant *Staphylococcus aureus* in pig farms in Switzerland

Julia G. Kraemer<sup>a,b</sup>, João Pires<sup>b,d</sup>, Marianne Kueffer<sup>b</sup>, Eulalia Semaani<sup>c</sup>, Andrea Endimiani<sup>b</sup>, Markus Hilty<sup>b</sup>, Anne Oppliger<sup>a,\*</sup>

<sup>a</sup> Institut universitaire romand de Santé au Travail (Institute for Work and Health), Universities of Lausanne and Geneva, CH-1066 Epalinges-Lausanne, Switzerland

<sup>b</sup> Institute for Infectious Diseases, University of Bern, CH-3001 Bern, Switzerland

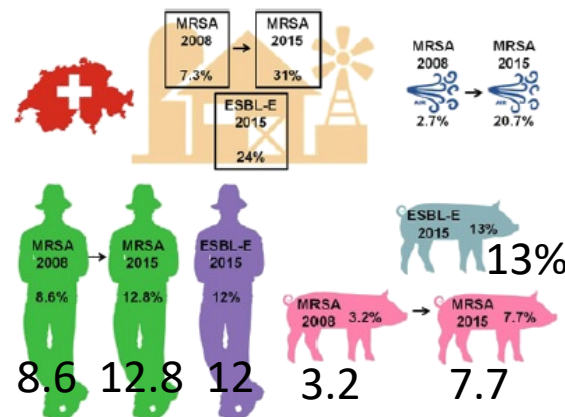
<sup>c</sup> SUIAG, SGD - SSP Berne - Suisse Romande, CH-1350 Orbe, Switzerland

<sup>d</sup> Graduate School for Cellular and Biomedical Sciences, University of Bern, CH-3001 Bern, Switzerland

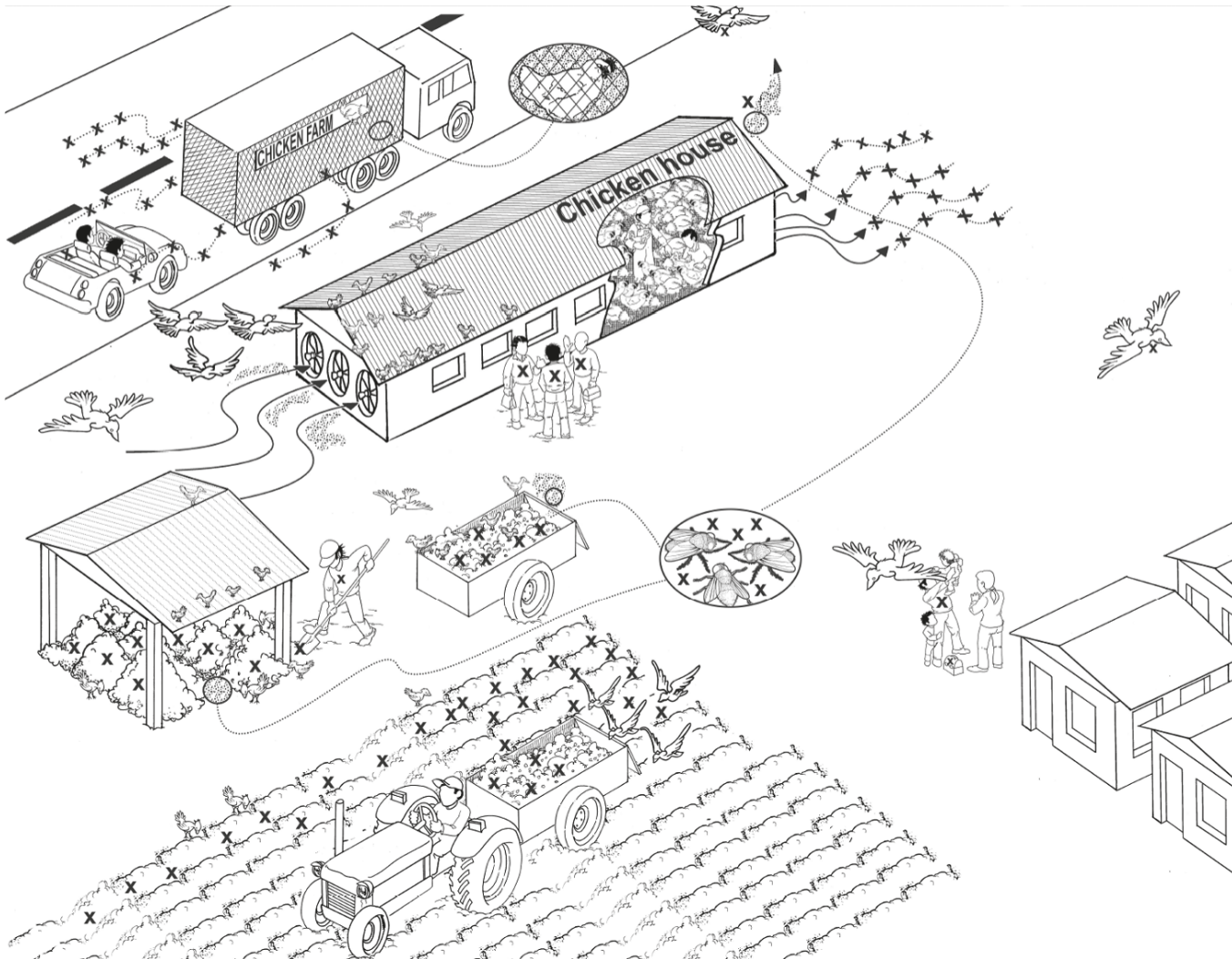
#### HIGHLIGHTS

- Antibiotic resistance in animal farms is a growing concern worldwide.
- Pig farms in Switzerland were screened for MRSA and ESBLE.
- MRSA (31%) and ESBLE (24%) were found in the investigated farms.
- MRSA prevalence increased in 2015, compared to 2008.

#### GRAPHICAL ABSTRACT



# Antibiotikaresistenz



A schematic representation (not to scale) of multiple potential pathways for exposure to and transfer of pathogens within the environs of concentrated animal feeding operations. From: Graham et al. 2008 . Public Health Reports. The Animal-Human Interface and Infectious Disease in Industrial Food Animal Production: Rethinking Biosecurity and Biocontainment.

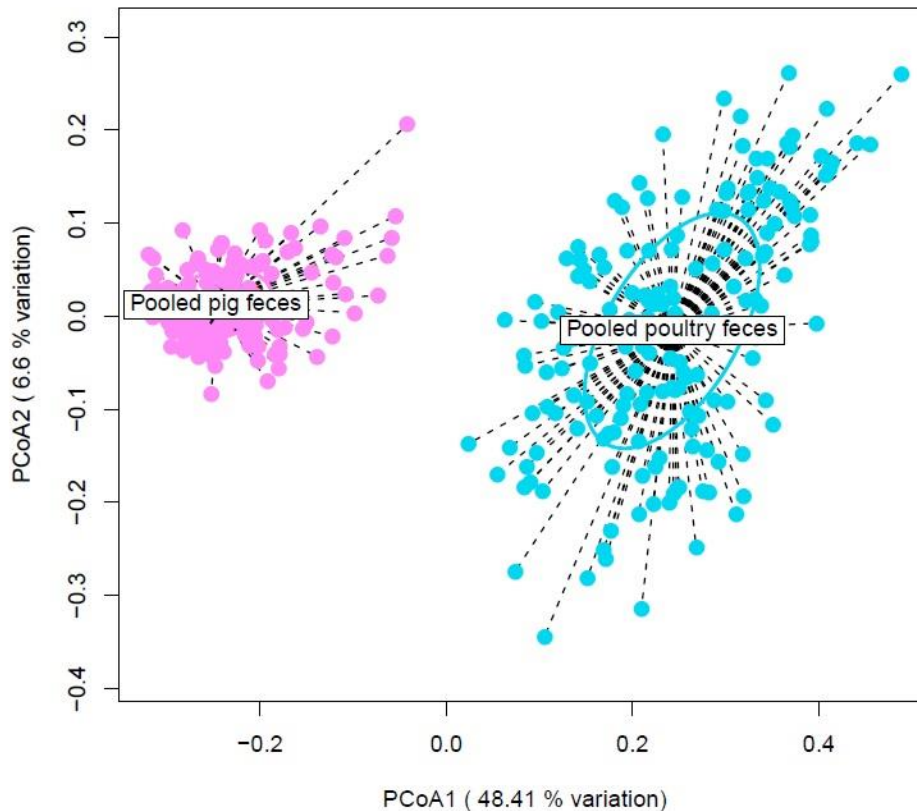




## Ecology from Farm to Fork Of microbial drug Resistance and Transmission

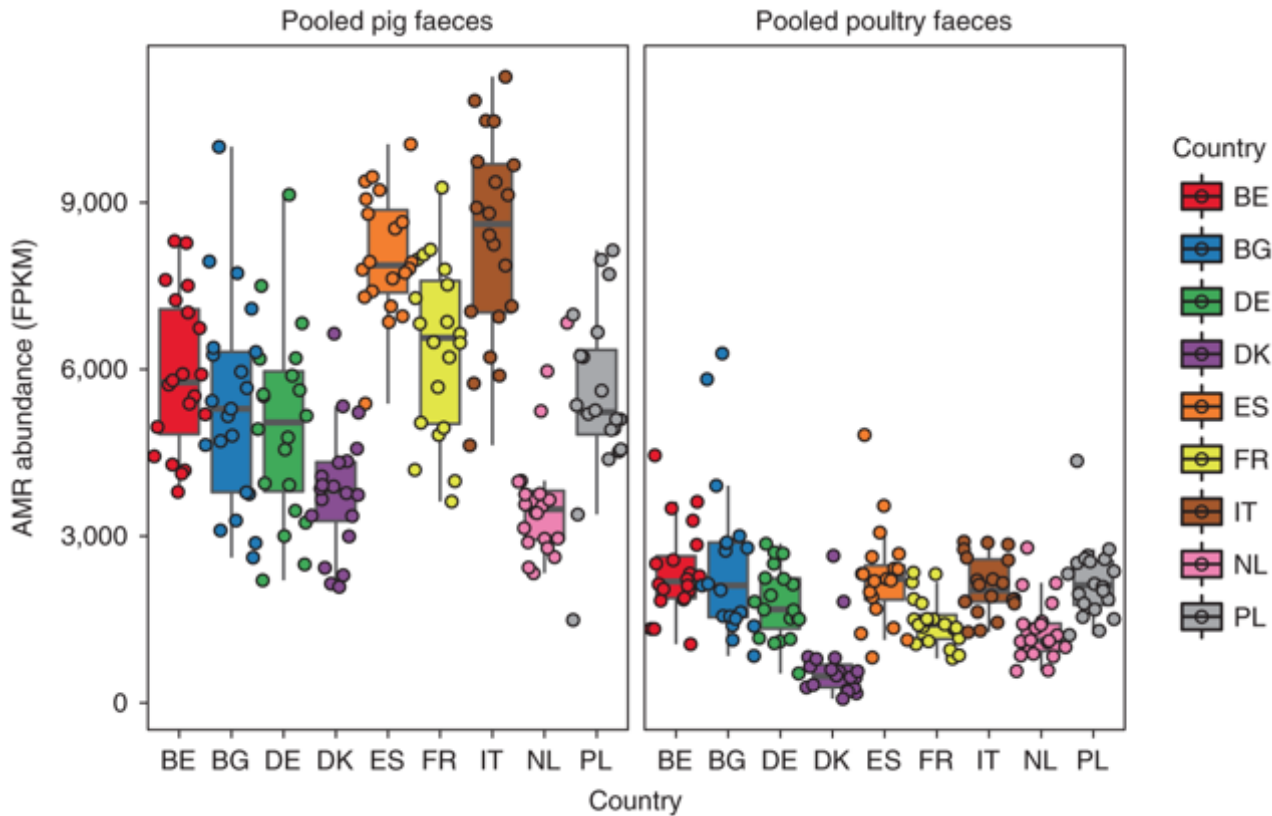
# Antibiotikaresistenz

- Antimicrobial Resistance (AMR) Genes
  - Häufig nur AMR, cave!
- Abbildung rechts:
  - Bislang grösste ARG Monitoring-Studie > 9,000 Tiere, 181 Schweine- und 178 Geflügelherden, 9 Länder



Munk P. *et al.* 2018. Abundance and diversity of the faecal resistome in slaughter pigs and broilers in nine European countries. *Nat Microbiol* 3, 898-908

- höchste Werte: Italien Schweine, niedrigste Werte: Dänemark Geflügel

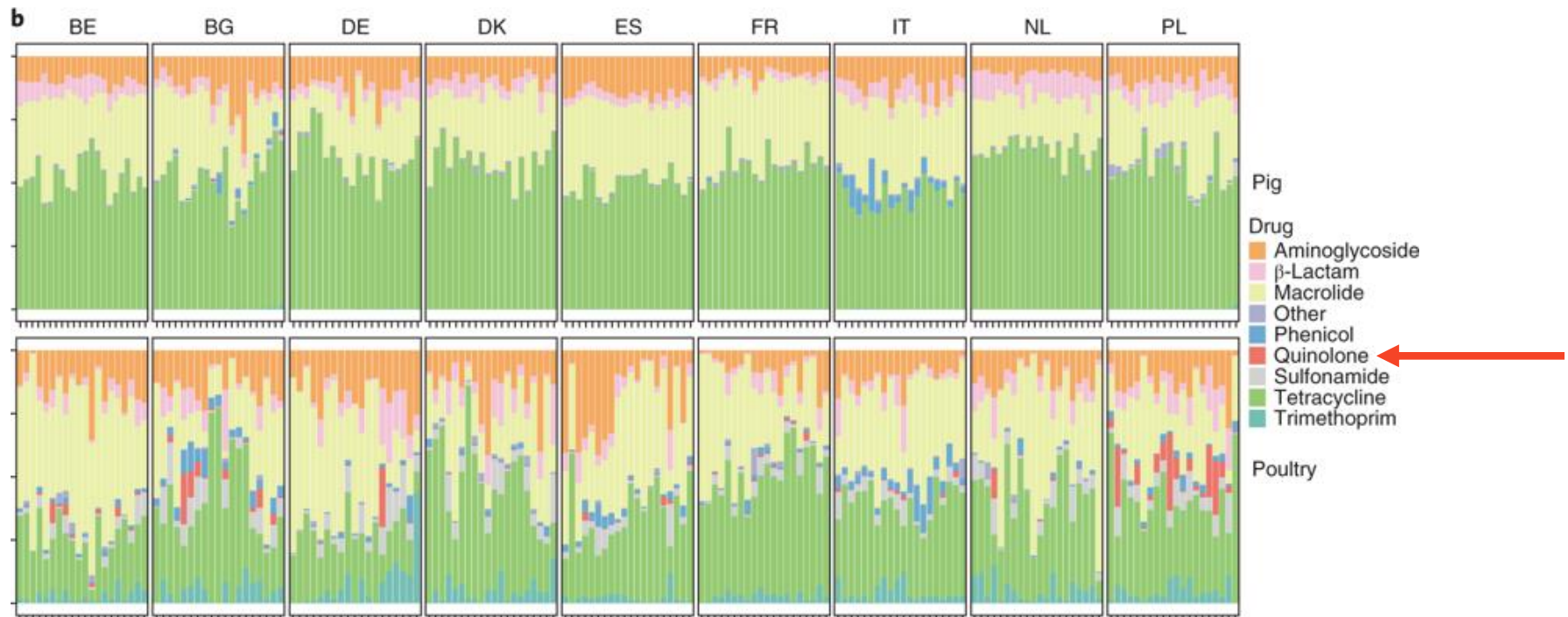


Munk P. *et al.* Abundance and diversity of the faecal resistome in slaughter pigs and broilers in nine European countries. *Nat Microbiol* 3, 898-908



# Antibiotikaresistenz

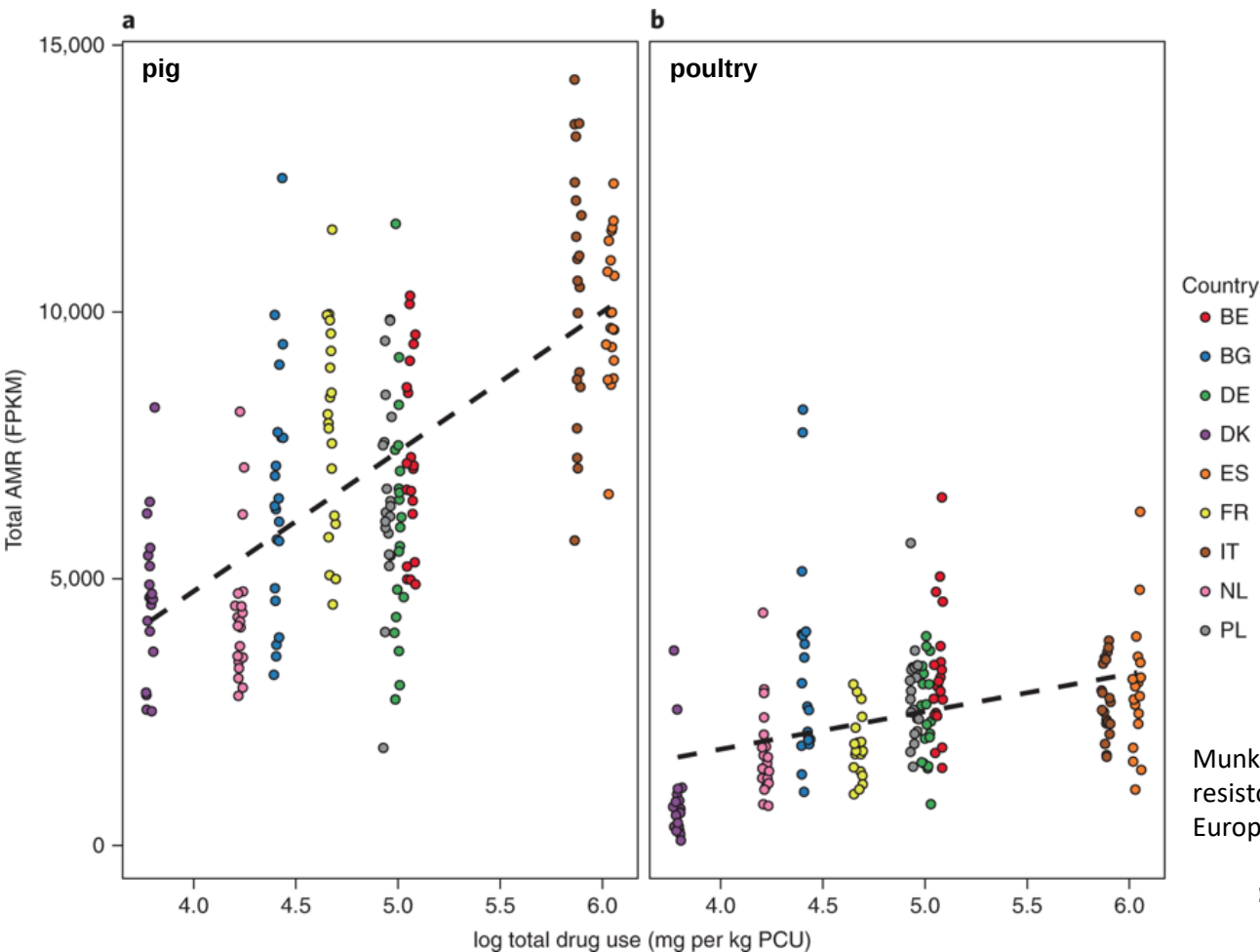
- relative Häufigkeit von ARG nach Antibiotika-Klassen
  - Schweineproben homogener
    - Häufigste Resistenz gegen Tetrazykline
  - Geflügelproben heterogener
    - Häufigste Resistenz gegen Tetrazykline, Makrolide,  $\beta$ -Laktam-, Aminoglykosidantibiotika



Munk P. *et al.* Abundance and diversity of the faecal resistome in slaughter pigs and broilers in nine European countries. *Nat Microbiol* 3, 898-908

# Antibiotikaresistenz

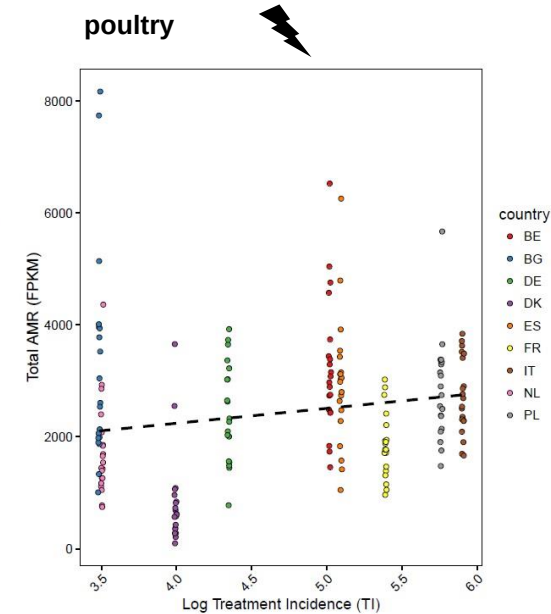
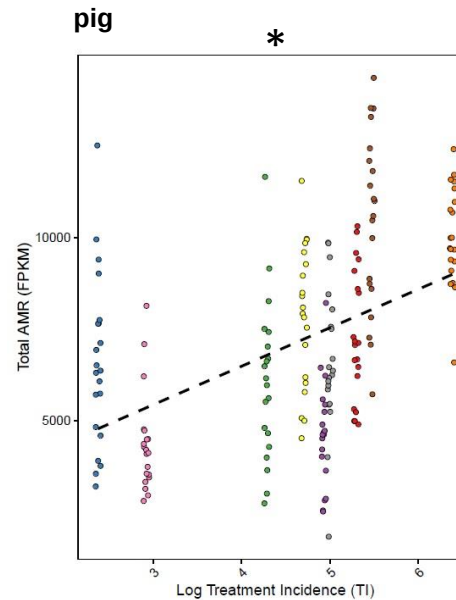
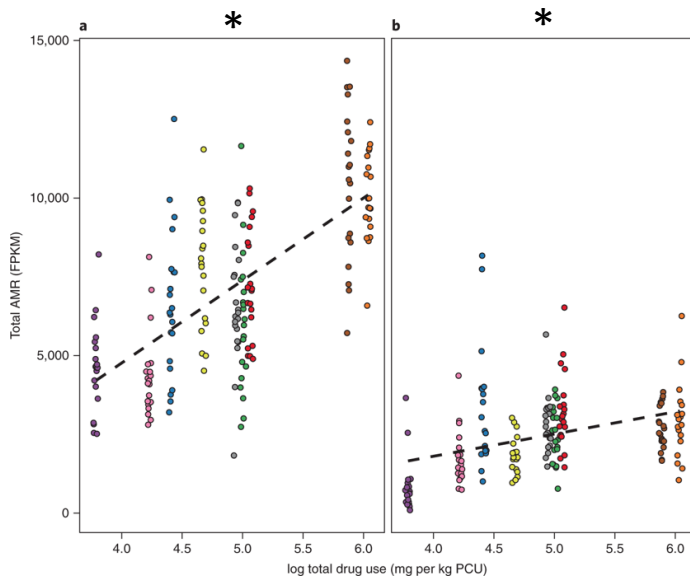
- Positive Korrelation Antibiotikaverbrauch
  - National veterinary antimicrobial usage European Medicines Agency's European Surveillance of Veterinary Antimicrobial Consumption (ESVAC)



Munk P. *et al.* Abundance and diversity of the faecal resistome in slaughter pigs and broilers in nine European countries. *Nat Microbiol* 3, 898-908

# Antibiotikaresistenz

- Positive Korrelation Antibiotikaverbrauch
  - Zusammenhang zwischen Behandlungsinzidenz und totaler AMR Gene der beprobten Herden.





- Für die Überwachung von AMR Genen gut geeignet
- Nachteile
  - nicht phänotypische Resistenz
  - Standardisierung
  - Sehr aufwendig

## Tiermodell

- Einsatz von Tieren in Experimenten als 'Modelle' für Menschen
- Bei jedem Forschungsprojekt muss das spezifische Modell sorgfältig ausgewählt werden.
- Modelle sollen dem modellierten Original ähneln
- gastrointestinale Krankheiten: *fecal microbiota transplantation* (FMT) mögliche neue Behandlungsmethode
  - Faktoren: genetische Prädisposition, Umweltfaktoren, Essstörungen, Stress, Immunkrankheiten und Mikrobiota
  - Bereits bei *Clostridium difficile* und chronisch-entzündlicher Darmerkrankung (IBD) als erfolgreich beschrieben
  - Ulzerative Kolitis chronische unspezifische Entzündung in Kolon und Rektum

- *fecal microbiota transplantation (FMT)*



Tiermodell

frontiers  
in Microbiology

ORIGINAL RESEARCH  
published: 24 August 2018  
doi: 10.3389/fmicb.2018.01921



Submit a Manuscript: <http://www.wjgnet.com/esps/>  
Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>  
DOI: 10.3748/wjg.v20.i40.14805

World J Gastroenterol 2014 October 28; 20(40): 14805-14820  
ISSN 1007-9327 (print) ISSN 2219-2840 (online)  
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REVIEW

## Intestinal microbiota pathogenesis and fecal microbiota transplantation for inflammatory bowel disease

Zi-Kai Wang, Yun-Sheng Yang, Ye Chen, Jing Yuan, Gang Sun, Li-Hua Peng

## Fecal Microbiota Transplantation Ameliorates Experimentally Induced Colitis in Mice by Upregulating AhR

Yan-Ling Wei, Yu-Qin Chen, Hao Gong, Ning Li, Kang-Qi Wu, Wang Hu, Bin Wang, Kai-Jun Liu, Liang-Zhi Wen, Xiao Xiao\* and Dong-Feng Chen\*

Dig Dis Sci (2016) 61:2262–2271  
DOI 10.1007/s10620-016-4060-2

ORIGINAL ARTICLE

## Beneficial Effects of Fecal Microbiota Transplantation on Ulcerative Colitis in Mice

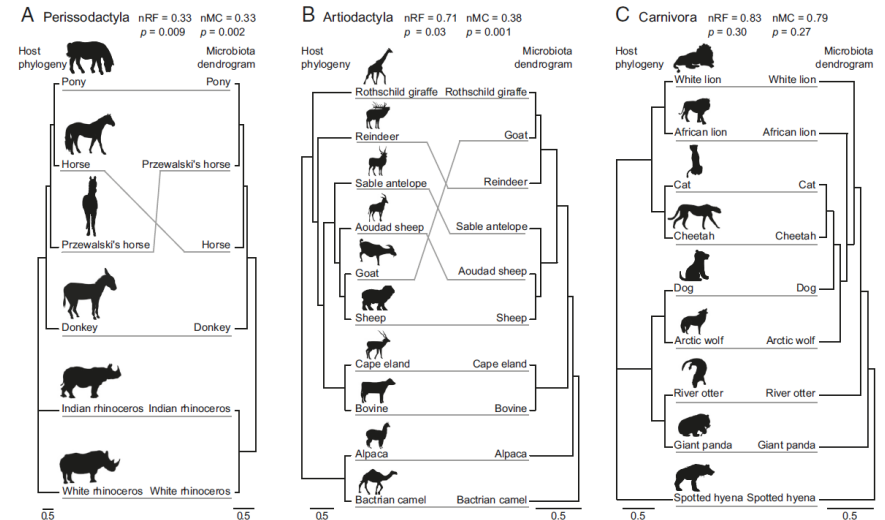
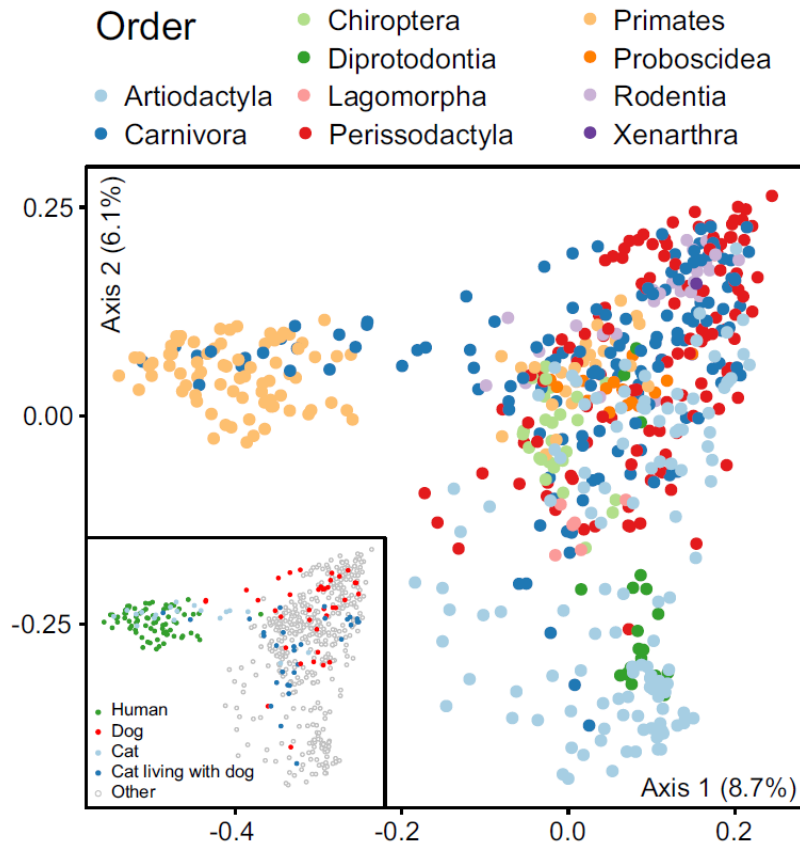
Zhihui Tian<sup>1</sup> · Jie Liu<sup>1</sup> · Mengyu Liao<sup>1</sup> · Wenjuan Li<sup>1</sup> · Jiaqi Zou<sup>1</sup> ·  
Xinxin Han<sup>1</sup> · Mingjie Kuang<sup>1</sup> · Wanqiu Shen<sup>2</sup> · Haidong Li<sup>1</sup>

## Peroral Low-Dose *Toxoplasma gondii* Infection of Human Microbiota-Associated Mice — A Subacute Ileitis Model to Unravel Pathogen–Host Interactions

Markus M. Heimesaat\*, Ulrike Escher, Anne Grunau, Ulrike Fiebiger and Stefan Bereswill

Charité — Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Microbiology and Infection Immunology, Berlin, Germany

- Hautmikrobiota
- Mensch anders



Dendrograms for species-specific skin microbiota generated using the Bray–Curtis distance metric and a 99% OTU threshold, compared with the known host phylogenies of Perissodactyla (A), Artiodactyla (B), and Carnivora (C).

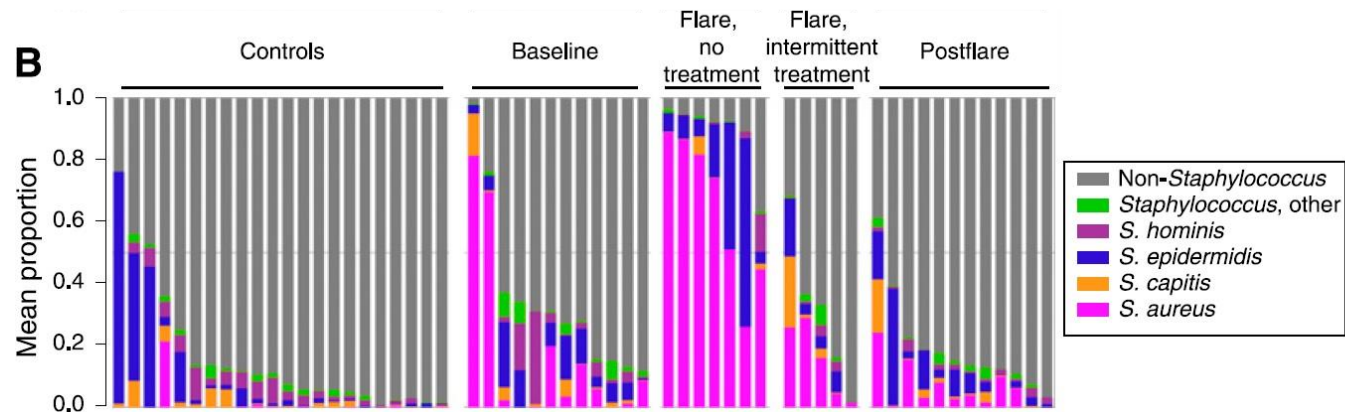
Ross et al. 2018 Comprehensive skin microbiome analysis reveals the uniqueness of human skin and evidence for phylosymbiosis within the class Mammalia  
doi:10. 1073/pnas.1801302115



- Neurodermitis (atopische Dermatitis)

## Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis

Heidi H. Kong,<sup>1,8</sup> Julia Oh,<sup>2</sup> Clay Deming,<sup>2</sup> Sean Conlan,<sup>2</sup> Elizabeth A. Grice,<sup>2</sup>  
Melony A. Beatson,<sup>1</sup> Effie Nomicos,<sup>1</sup> Eric C. Polley,<sup>3</sup> Hirsh D. Komarow,<sup>4</sup> NISC Comparative  
Sequence Program,<sup>5,7</sup> Patrick R. Murray,<sup>6</sup> Maria L. Turner,<sup>1</sup> and Julia A. Segre<sup>2,8</sup>

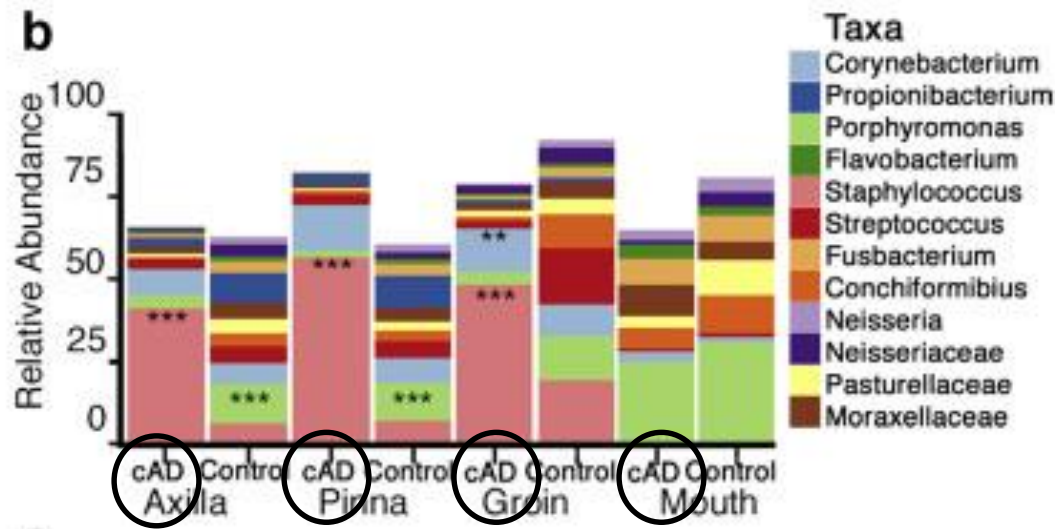


- Canine atopische Dermatitis

## Longitudinal Evaluation of the Skin Microbiome and Association with Microenvironment and Treatment in Canine Atopic Dermatitis



Charles W. Bradley<sup>1</sup>, Daniel O. Morris<sup>2</sup>, Shelley C. Rankin<sup>1</sup>, Christine L. Cain<sup>2</sup>, Ana M. Mistic<sup>1</sup>, Timothy Houser<sup>3</sup>, Elizabeth A. Mauldin<sup>1</sup> and Elizabeth A. Grice<sup>4</sup>

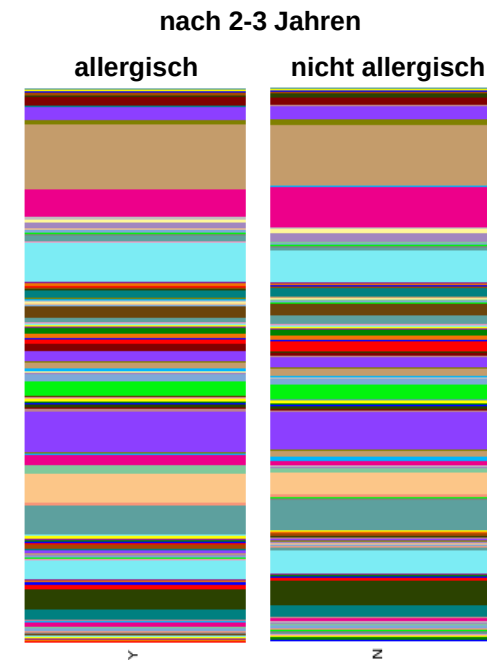
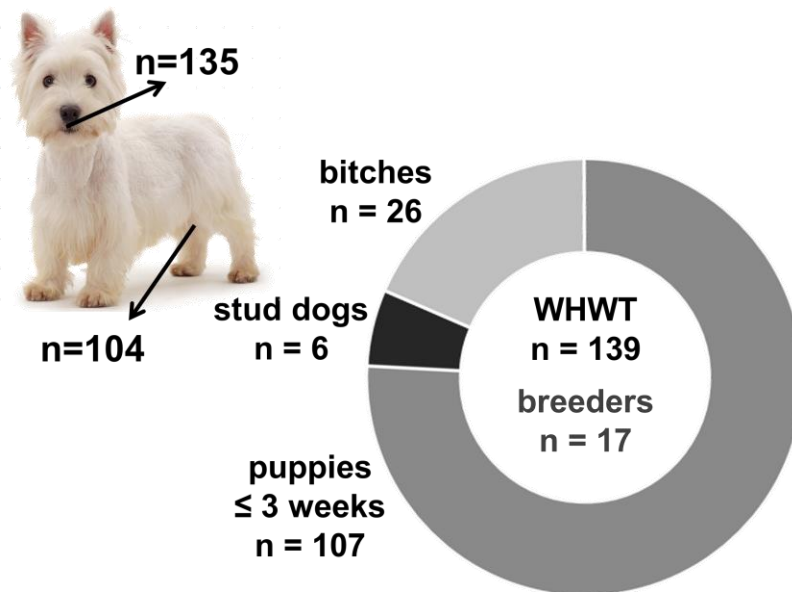


- Prädisposition bestimmter Rassen



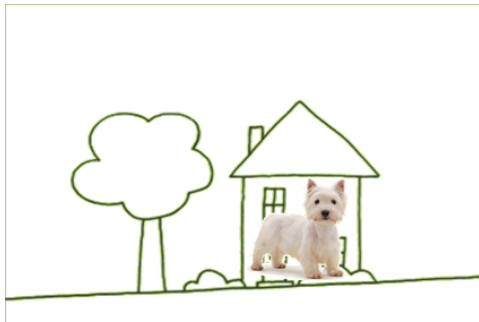
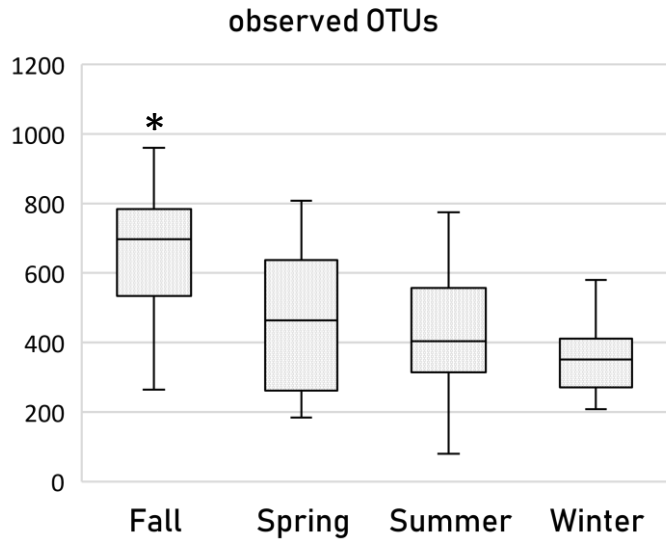
## Canine and Human Atopic Dermatitis: Two Faces of the Same Host-Microbe Interaction

Domenico Santoro<sup>1,3</sup> and Aline Rodrigues Hoffmann<sup>2,3</sup>



Rodriguez-Campos S., Rostaher A., Zwickl L., Fischer N., Vidal S., Brandt B.W., Favrot C., Perreten V.

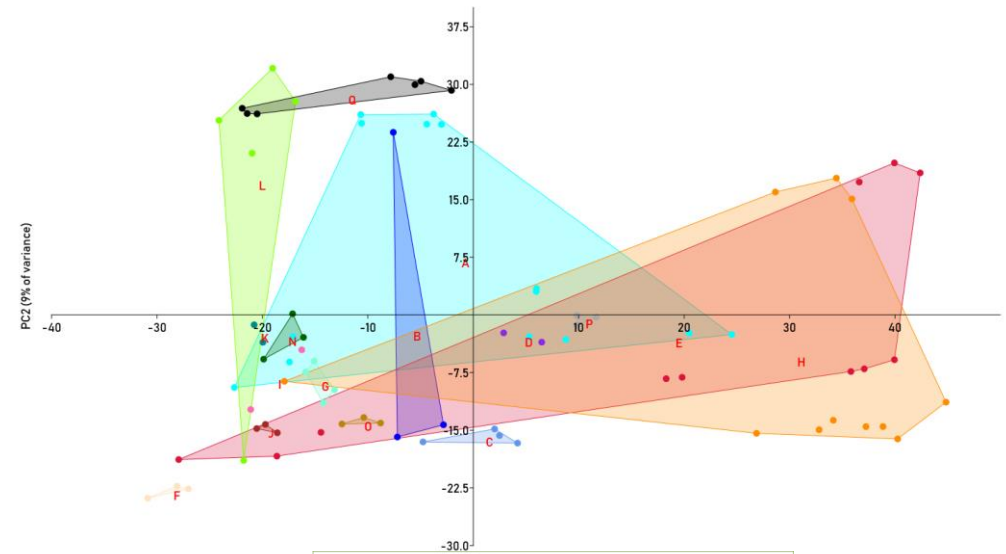
**Unveröffentlicht!**



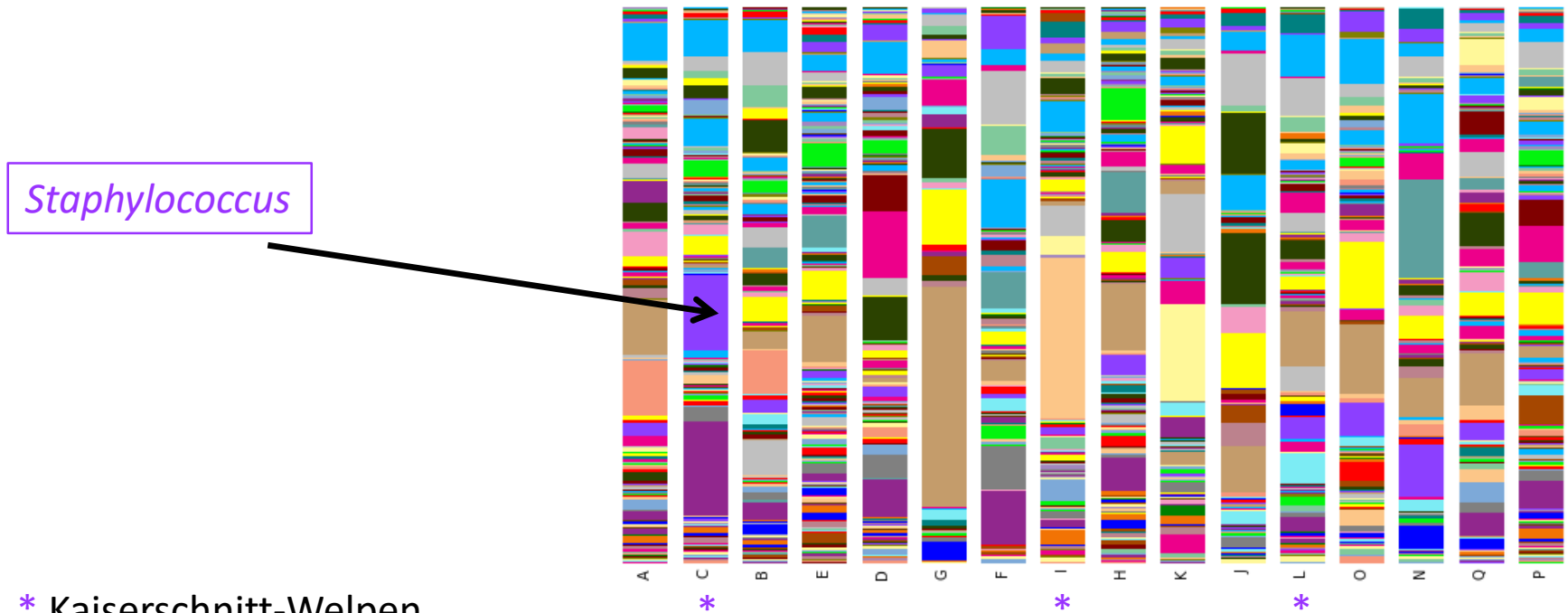
$p < 0.05$



PCA gruppiert nach Besitzer



## Genus – Welpen Haut



\* Kaiserschnitt-Welpen

Rodriguez-Campos S., Rostaher A., Zwickl L., Fischer N., Vidal S., Brandt B.W., Favrot C., Perreten V.

Unveröffentlicht!

- 
- Modelle sollen dem modellierten Original ähneln
  - Das Modell muss gut studiert werden bevor Ergebnisse extrapoliert werden können
  - Ausreichende Probenzahl
  - Standardisierte Umwelt, da viele Störfaktoren
  - Neue Therapiemethoden?

Produktion

- Ausnutzen der Kenntnisse über eine gesunde Mikrobiota (Mikrobiom), um gesündere und/oder ertragsreichere Zucht/Mast
- Darmmikrobiom
- Am meisten Studien: Fisch
  - Unterschiede Anatomie
  - Wassertemperatur
  - Wild / Zucht
- Probiotika “lebende Mikroorganismen, die, wenn in adäquaten Dosen verabreicht, einen Vorteil für die Gesundheit schaffen” (WHO and FAO, 2006)



REVIEW  
published: 04 May 2018  
doi: 10.3389/fmicb.2018.00873

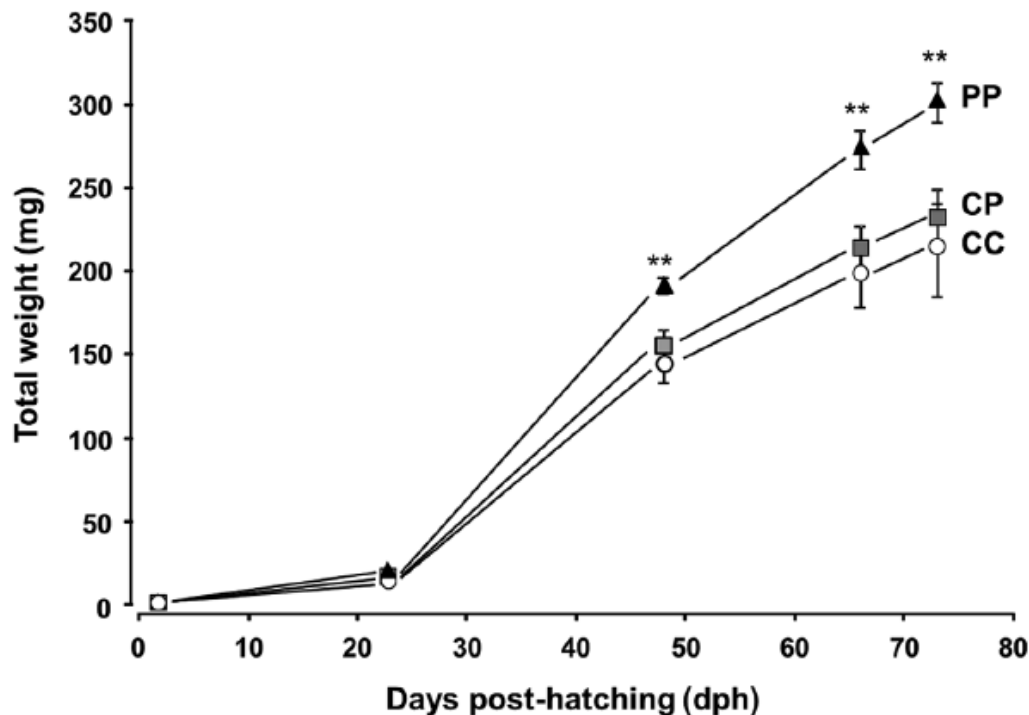


## The Gut Microbiota of Marine Fish

Sian Egerton<sup>1,2</sup>, Sarah Culloty<sup>2,3</sup>, Jason Whooley<sup>4</sup>, Catherine Stanton<sup>5,6</sup> and R. Paul Ross<sup>1,5,6\*</sup>

<sup>1</sup> School of Microbiology, University College Cork, Cork, Ireland, <sup>2</sup> School of Biological, Earth and Environmental Sciences, University College Cork, Cork, Ireland, <sup>3</sup> Environmental Research Institute, University College Cork, Cork, Ireland, <sup>4</sup> Bio-marine Ingredients Ireland Ltd., Killybegs, Ireland, <sup>5</sup> Teagasc Research Centre, Fermoy, Ireland, <sup>6</sup> APC Microbiome Ireland, Teagasc and University College Cork, Cork, Ireland

- Ausnutzen der Kenntnisse über eine gesunde Mikrobiota (Mikrobiom), um gesündere und/oder ertragsreichere Zucht/Mast



control diet (CC)  
diet supplemented with probiotic SpPdp11  
from 10 to 21 dph (CP)  
from 2 to 21 dph (PP)

Jurado et al. 2018. Dietary administration of the probiotic *Shewanella putrefaciens* Pdp11 promotes transcriptional changes of genes involved in growth and immunity in *Solea senegalensis* larvae. Fish and Shellfish Immunology. doi.org/10.1016/j.fsi.2018.04.018



**Table 1.** Microbiome-based products for conditioning of water and pond as well as promotion of a healthy production animal microbiome (feed and feed additives).

| Target environment | Company           | Product                         | Purpose                                                                                            | Composition                                                                             | Reference |
|--------------------|-------------------|---------------------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-----------|
| Water and pond     | AqualnTech        | PRO4000X, AquaPro B, AquaPro EZ | Degrade organic matter, reduce ammonia, <i>Vibrio</i> reduction                                    | 2 Strains of <i>Bacillus</i> – <i>Bacillus subtilis</i> , <i>Bacillus licheniformis</i> | 1, 2, 3   |
|                    | Biomin            | Aquastar                        | Stabilize water quality, improve pond bottom quality and support the gut health of fish and shrimp | Formula not publicly available                                                          | 4         |
|                    | Keeton Industries | Waste & Sludge Reducer          | Improve water and bottom quality, pathogen control                                                 | <i>Bacillus cereus</i> RRRL B-30535                                                     | 5, 6      |
|                    | Keeton Probiotics | ShrimpShield, PondToss          | Degrade organic sludge, improve feed efficiency                                                    | Formula not publicly available                                                          | 7, 8      |
|                    | Lallemand         | Lalsea Biorem                   | Degrade organic matter, reduce ammonia, pathogen control, stabilize pH                             | 7 specific bacterial strains                                                            | 9         |
|                    | Novozymes         | Pond Plus                       | Pathogen control, decomposition of organic                                                         | Spore forming bacteria                                                                  | 10        |

Dittmann et al. 2018. The aquaculture microbiome at the centre of business creation doi:10.1111/1751-7915.12877

Antibiotika-  
resistenz



RESEARCH ARTICLE

# Extended antibiotic treatment in salmon farms select multiresistant gut bacteria with a high prevalence of antibiotic resistance genes

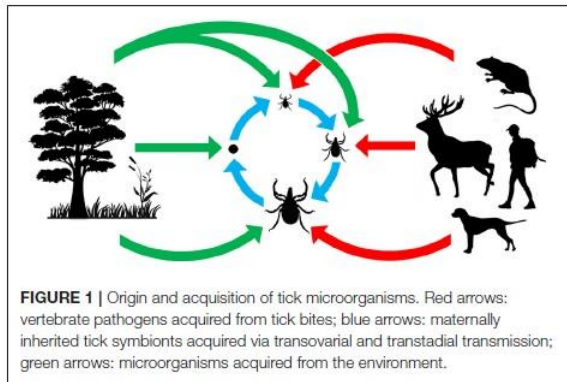
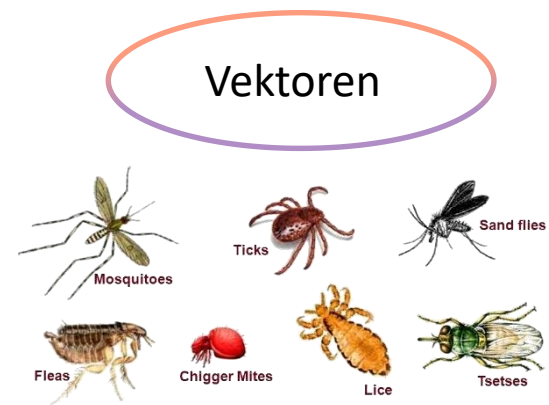
Sebastián Higuera-Llantén<sup>1</sup>, Felipe Vásquez-Ponce<sup>1</sup>, Beatriz Barrientos-Espinoza<sup>1</sup>, Fernando O. Mardones<sup>2</sup>, Sergio H. Marshall<sup>1</sup>, Jorge Olivares-Pacheco<sup>1,3\*</sup>

- Nicht nur wirtschaftlicher Aspekt
- Auch Verbesserung der Tiergesundheit und damit des Tierwohls



# Vektoren

- Stechmücken: Zikavirus, Dengue, West Nile, Malaria
  - Zecken: Lyme-Borreliose, Tularämie, FSME, Q-Fieber
  - Sandfliegen bzw. -mücken: Leishmaniose, Peru-Warzen, Phlebotomusfieber
  - Flöhe: Pest, Katzenkratzkrankheit (cat scratch fever), Hundebandwurm, murines Fleckfieber, endemischer Typhus
  - Läuse: murines Fleckfieber, Schützengrabenfieber, Rückfallfieber
  - *Reversed discovery of disease* (Tijssen-Klasen et al 2014)
  - Nicht nur Pathogene, auch Symbionten
  - Einfluss der Symbionten auf Pathogene
- neue Kontrollstrategien



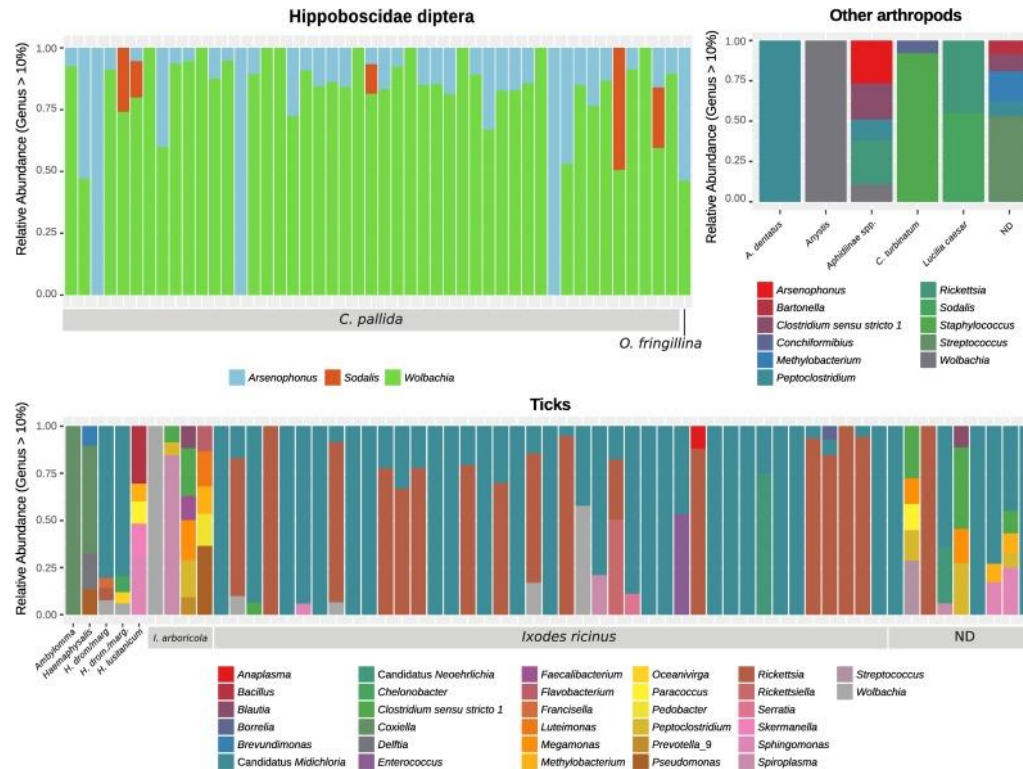
Bonnet et al. 2017 doi: 10.3389/fcimb.2017.00236



[www.commonswiki.org](http://www.commonswiki.org) File:World-airline-routemap-2009.png



# Vektoren



115 Wandervögel (Italien)

194 Ektoparasiten

Gruppiert: Lausfliegen, Zecken, andere

| Genus              | MSR Prevalence      | PCR prevalence      |
|--------------------|---------------------|---------------------|
| <b>Rickettsia</b>  | 94.8% (88.94–97.84) | 40.5% (32.02–49.62) |
| <b>Ehrlichia</b>   | 84.5% (76.71–90.04) | -                   |
| <b>Borrelia</b>    | 14.7% (9.26–22.32)  | 8.6% (4.59–15.31)   |
| <b>Coxiella</b>    | 5.2% (2.16–11.06)   | 0%                  |
| <b>Francisella</b> | 3.4% (1.06–8.82)    | 1.7% (0.09–6.46)    |
| <b>Bartonella</b>  | 3.4% (1.06–8.82)    | 0%                  |
| <b>Anaplasma</b>   | 2.6% (0.55–7.66)    | 1.7% (0.09–6.46)    |

Cerutti et al., 2018 PLoS One. The microbiota of hematophagous ectoparasites collected from migratory birds.  
doi: 10.1371/journal.pone.0202270

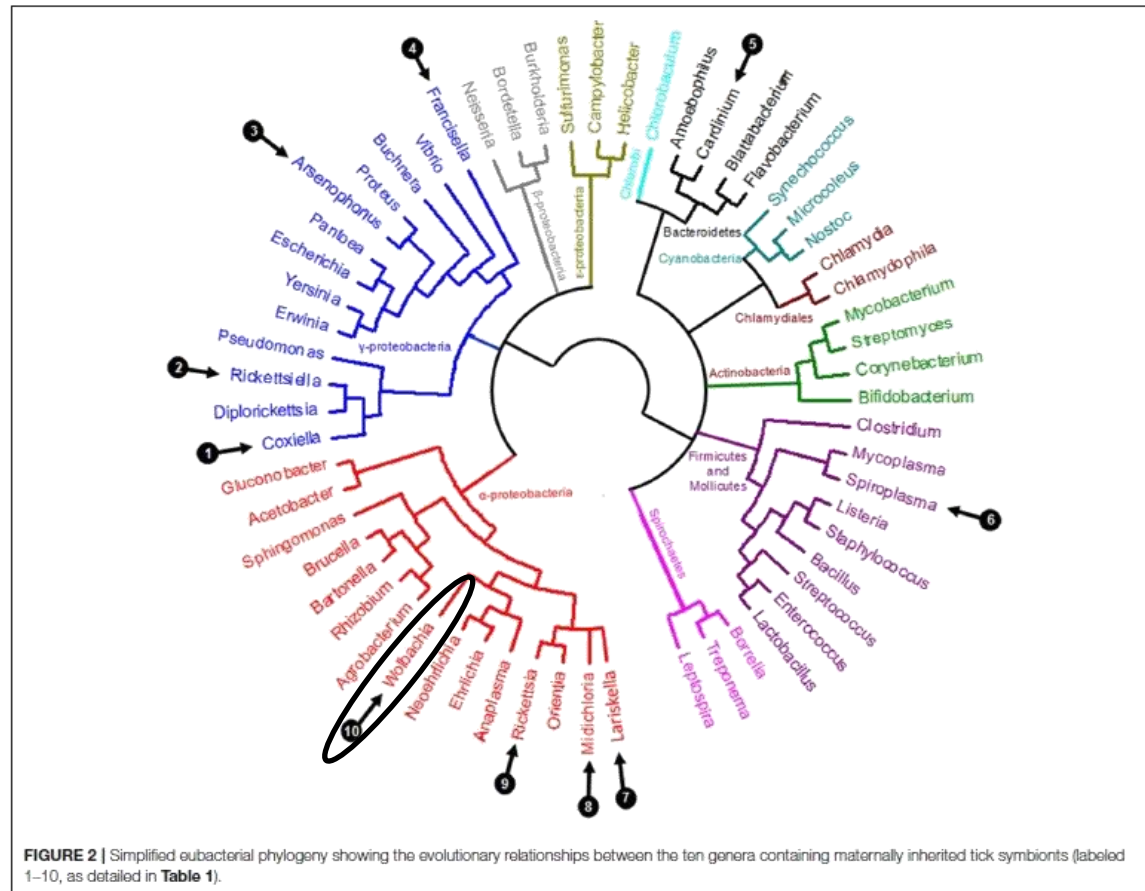
# Vektoren

- Symbionten

z.B. Zecken *Coxiella*-like endosymbionts (LE), *Francisella*-LE, *Rickettsia peacocki*

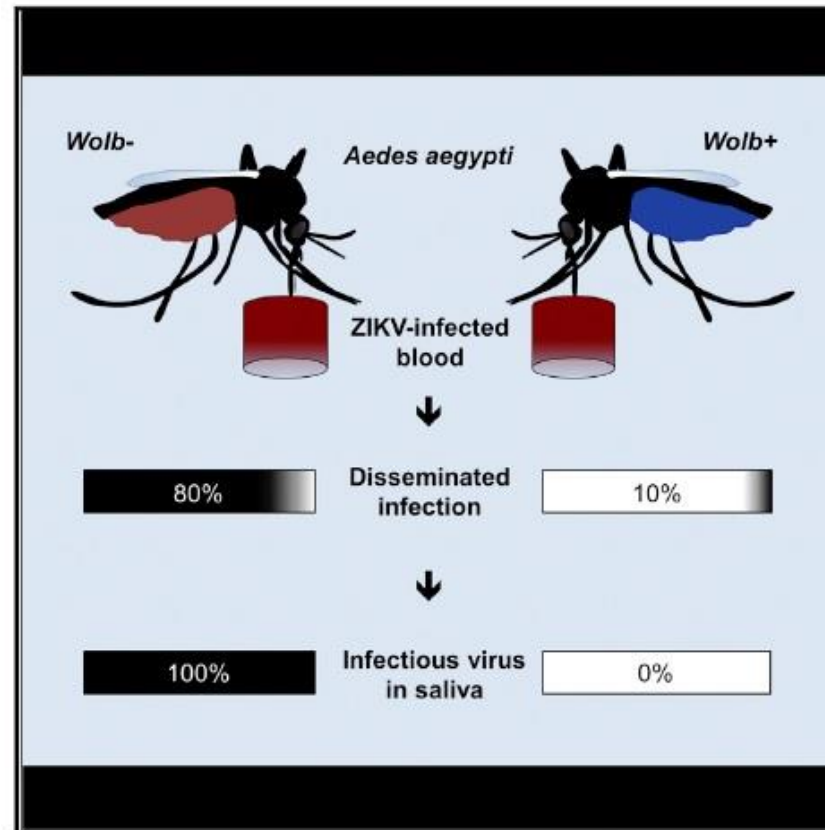
1. Nicht-Pathogene stehen in Konkurrenz mit Pathogenen um Nährstoffe
2. Nicht-Pathogene positiven/negativen Einfluss auf das Wachstum der Pathogene

*Wolbachia*



Bonnet et al. 2017 doi: 10.3389/fcimb.2017.00236

*Wolbachia*



Dutra et al. 2016 Cell Host & Microbe Wolbachia Blocks Currently Circulating Zika Virus Isolates in Brazilian *Aedes aegypti* Mosquitoes 19, 771–774 doi.org/10.1016/j.chom.2016.04.021



**Gruppe PD Dr. Paola Pilo**

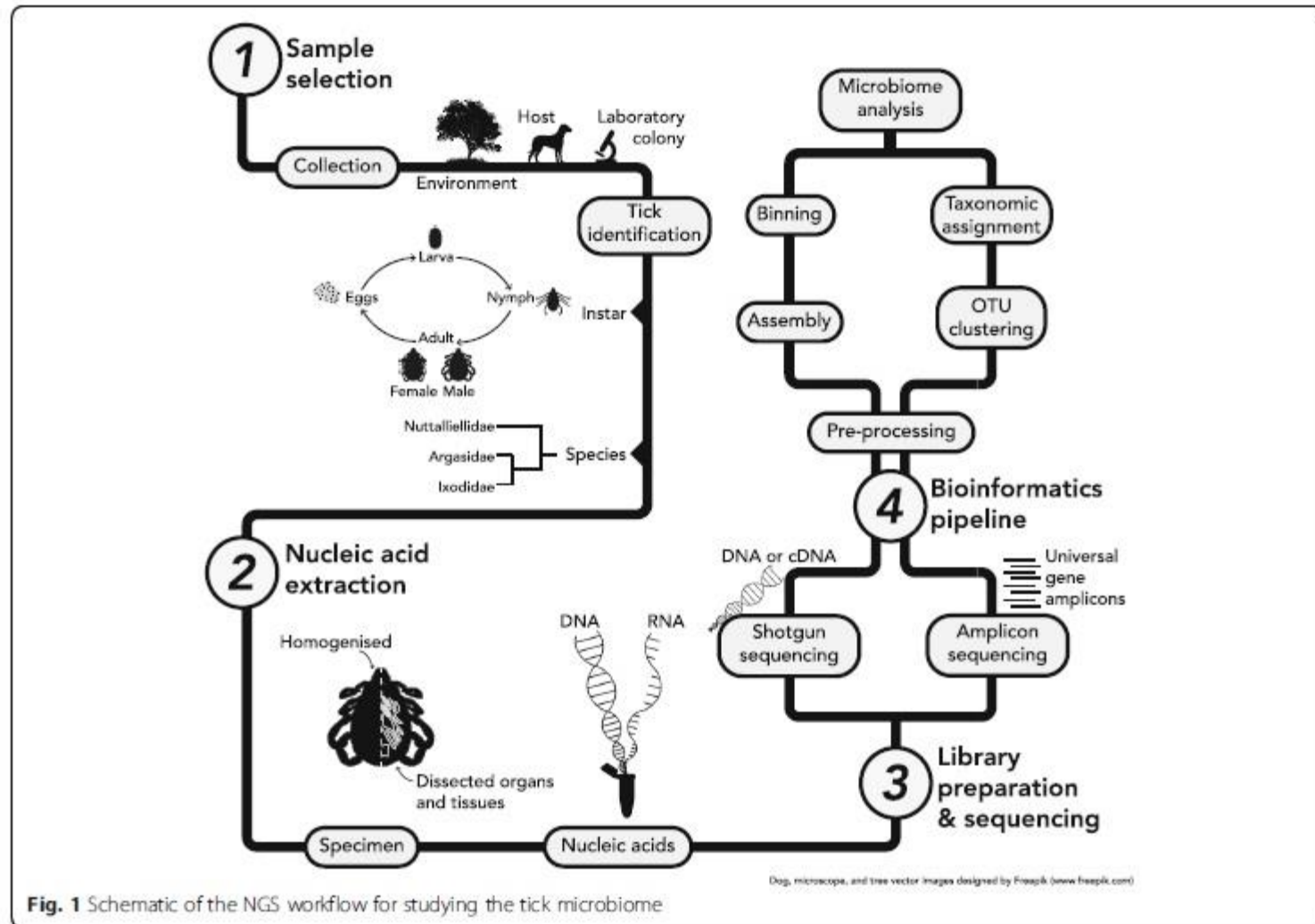
paola.pilo@vetsuisse.unibe.ch

Unveröffentlicht! (Bildmaterial entfernt)

Schweizer Studie in einem kontrollierten Mäusebestand

3 Jahre zuvor Ausbruch Tularämie

Probensammlung Flöhe → Mikrobiotaanalyse



**Fig. 1** Schematic of the NGS workflow for studying the tick microbiome

Gray et al. 2018. Parasites & Vectors 11:12. Recent insights into the tick microbiome gained through next-generation sequencing  
doi: 10.1186/s13071-017-2550-5

# Abschlussbemerkungen

- Mehr *coverage* als gezielte PCRs
  - für spezielle Fragen nach konkreten Keimen: PCR
- Gute Probenahmestrategie notwendig
- Harmonisierung/Standardisierung zwischen Laboren schwierig
  - Studien nur bedingt vergleichbar
  - Systematische Fehler möglich, z.B. bei PCR-abhängigen Methoden
- Möglichkeit neue oder bislang vernachlässigte Keime zu entdecken
- Kosten
  - Weniger für Amplikonsequenzierung
  - Mehr für Shotgun-Sequenzierung

# Das tierische Mikrobiom: Erkenntnisse für die Schnittstelle Mensch-Tier

Antibiotika-  
resistenz



Nutztiere



Zoonosen



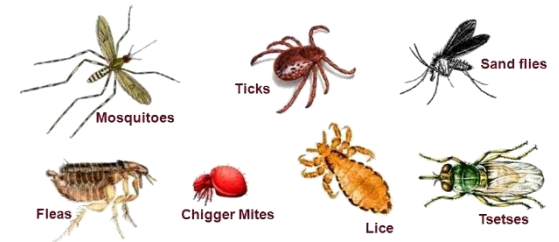
Produktion



Tiermodell



Vektoren



Danke fürs Zuhören!

Fragen?

